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SUMMARY OF RECENT ABSTRACTS*

IV. TRYPANOSOMIASIS

General: Epidemiology

The report on the Inter-Colonial Conference on Trypanosomiasis (p. 584), which was convened in Lourenço Marques in 1946, contains much information on the distribution of *Glossina* and the trypanosome diseases of man and animals, methods of control (such as game destruction in S. Rhodesia and the use of DDT sprayed by airplane) and clinical subjects. It is not a collection of papers describing new work so much as a series of statements of the position existing at the time. In 1948 a conference on tsetse and trypanosomiasis was held at Brazzaville, and was attended by representatives of the different countries. GEAR (p. 770) has written a short general account of this conference.

PINTO (p. 1070) reports on a survey of Portuguese Guinea in which 12,443 persons were examined and 248 cases of trypanosomiasis were detected.

Aetiology

FAIRBAIRN (p. 50) discusses the results of infecting rats with *T. rhodesiense* taken from man early in the disease, in relation to the types of trypanosomes (as regards length) and their electrical charge. He believes that trypanosomes whose length is above the mean are mature, that they alone can enter into syngamy and produce infection, and that both negatively and positively charged forms are necessary for infection, and he describes the experiments on which these opinions are based. In comment, BROOM makes certain criticisms of the work, and these should be sought in the original.

VANDERPLANK (p. 413) infected wart-hogs and elands with *T. rhodesiense*, and showed that the trypanosomes remained in their blood for long periods.

SANDGROUND (p. 585) has succeeded, by inoculation of nursling rats, in enhancing the virulence of a strain of *T. gambiense*, and in changing its susceptibility to drugs and its general behaviour so that it became indistinguishable from *T. brucei*. In this state the strain remained stable. He argues that similar changes may take place in nature, and he holds the view, which agrees with the opinion previously expressed by HOARE, that *T. gambiense* and *T. rhodesiense* are mutant strains of a single species which the laws of zoological nomenclature would by reason of priority recognize as *T. brucei*.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1948, v. 45. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

VAN HOOF *et al.* (p. 503) have studied *T. brucei* in the Belgian Congo where, in areas in which *G. palpalis* predominates, it has been found in dogs, pigs and goats. *T. brucei* is more abundant than *T. gambiense* in the blood of pigs, and pigs probably serve as the best reservoir ; in dogs it produces a characteristic keratitis, and the dog may therefore be useful in differentiating *T. brucei* from the human trypanosomes. All attempts, except one, to infect man with *T. brucei* failed ; in this one there was transient appearance of the trypanosomes in the blood, but they could not be found later. This seems to indicate that some susceptible persons may carry *T. brucei* in nature, and that the trypanosome strains, perhaps modified to adapt to man, may be transmitted by tsetse from such people. In some such way, perhaps, a mutant strain of *T. brucei* may be produced which could affect man.

SICÉ (p. 312) reports that two laboratory workers in Switzerland became infected with *T. gambiense*, not, apparently, by accidental inoculation, but by contaminating their fingers with infected blood in the course of their experiments.

Transmission

HEGH (p. 275) has written a useful book on tsetse flies, with special reference to those of the Belgian Congo. NASH (p. 983) has published a booklet on tsetse which would be intelligible to Africans who have had only slight education.

JACKSON (p. 874) has carried a stage further his investigations on a tsetse-fly population in East Africa, and has noted short-term fluctuations in death rates and birth rates, which cannot be associated with climatic changes but appear to depend on factors in the fly population. Male *G. morsitans* are relatively inactive in the first two weeks of life and during this period their death rate may be low ; this has led the author to a re-calculation of the whole male population.

VANDERPLANK (p. 51) shows that if both males and females of *G. morsitans* and *G. swynnertoni* are kept together, random mating occurs between the species, and the females cross-inseminated produce either sterile eggs or pupae which develop into sterile hybrids. He thinks that this process probably occurs in nature where the two species overlap, and that it may be the basis of one means of control. He (p. 244) has investigated the feeding habits of *G. swynnertoni* and *G. pallidipes* in relation to intervals between feeds in different climatic conditions. Flies classed as very hungry carry reserves of food and water sufficient for two days or less, those classed as replete carried reserves for a week or more. The periods are shorter when humidity is low or evaporation high.

The same author (p. 413) has studied the incidence of trypanosomiasis in game in East Africa, and records the results of examining a large number of *G. swynnertoni* and *G. pallidipes* for animal trypanosomes.

CHORLEY (p. 771) has obtained evidence that *G. morsitans* and *G. pallidipes* are guided by their sense of smell more than is generally supposed, and that the smell of animal dung attracts them.

HORNBY (p. 1068) has written an account of *G. brevipalpis* and the types of vegetation in which it is found in southern Mozambique, and of a trypanosomiasis survey of cattle in the same area.

SCHWETZ (p. 484) reports a survey of Lake Tumba, in the Belgian Congo, in which he observed that *G. palpalis* was rare along the shores of the lake, but very prevalent along the banks of the rivers that flow into it.

NASH (p. 689) thinks that most sleeping sickness conveyed by *G. palpalis* and *G. tachinoides* in Nigeria is transmitted in the late dry season when soil temperature is high and when the flies have become restricted to permanent water such as village water holes, where contact with man is close. If this is so it may be possible to reduce the length and cost of protective clearings at river crossings, to that required for the dry season only.

The parasite of tsetse pupae, *Syntomosphyrum glossinae*, has been found by NASH (p. 245) in Nigeria.

GEIGY (p. 873) has described his technique for maintaining a culture of *G. palpalis* in Europe.

Control

BUXTON (p. 983) has summed up the known means of controlling tsetse.

At a conference held in Nairobi in 1947, under the auspices of the East Africa High Commission (p. 982) a resolution was adopted that the method of controlling *G. morsitans* by destruction of game should be tested in more varied conditions than exist in S. Rhodesia, and in relation to other tsetse flies, but that since clearing of fly is of little value unless full use is made of the land, plans should be made for settlement. Uncontrolled slaughter is condemned. The conference recognized the possibility that bush clearing, or the use of insecticides, or other methods now being studied, may prove better than destruction of game.

VAUGHAN-JONES (p. 879) gives a general account of the aims and functions of the Game and Tsetse Control Department of N. Rhodesia. In relation to *G. morsitans* the Department has used game exclusion or destruction methods and also selective clearing, and the results in general are encouraging.

DU TOIT (p. 52) describes the use of DDT smoke, emitted from the exhausts of low-flying aircraft, in the destruction of tsetse flies in South Africa. In this form, DDT will penetrate dense bush. He reports favourably on the method.

SYMES *et al.* (p. 588) have attempted the control of *G. palpalis* by spraying Gammexane or DDT on vegetation once or more than once. In each experiment there was a considerable reduction in fly density for some days, but the numbers of flies soon began to increase. There was much absorption of the insecticides by the vegetation. The authors conclude that the method is not satisfactory.

GLASGOW and DUFFY (p. 245) succeeded in eradicating *G. palpalis* completely from an isolated stretch of riverine bush in Kenya by hand-catching methods in which teams of boys, with hessian screens, were used. They make the point that hand-catching speedily reduces *G. palpalis* to a low density, and would therefore be expected to check an epidemic.

MCLETCHIE (p. 502) has given an account of the methods used to control sleeping sickness in Nigeria since 1925, when the hitherto quiescent disease began to spread extensively. He discusses the clinical types of *T. gambiense* infection, noting that the death rate may be high even where the disease appears to be mild. Treatment, which he outlines, is the first step in control, and is carried out by travelling teams and at dispensaries. Control of *G. palpalis* and *G. tachinoides* by clearing of streams, and in the Anchau corridor, are also described in this paper.

Clinical Findings

HARDING and HUTCHINSON (p. 410) describe the *T. gambiense* sleeping sickness observed in Sierra Leone, where an unusual form occurs in one area. In this form the trypanosomes are much more commonly found in blood than in gland fluid (which is most unusual in *T. gambiense* infections), and the disease is mild even in patients with increased cell count in the cerebrospinal fluid. Although up to one-third of the population had been infected, the population had not decreased. Elsewhere in Sierra Leone the disease is of more usual type.

Noting that most Africans have an erythrocyte sedimentation rate which is higher than the normal for Europeans, HOLLINS and LEWIS-FANNING (p. 1070) report on the rate observed in trypanosomiasis of man in Nigeria. Increase in the sedimentation rate is a feature of the disease, and corresponds roughly

with its severity. In trypanosomiasis a low rate indicates early infection or infection of low virulence. The authors think that if in a mass survey patients are found with high rates, but in whom trypanosomes cannot be found, they should be given a single injection of antrypol or pentamidine. If the rate has fallen when they are re-examined a month later, they should be regarded as having trypanosomiasis.

HILL (p. 874) gives his reasons for advocating the Sicard and Cantaloube method of measuring protein in the cerebrospinal fluid, and makes the point that as different methods lead to very different results, the method used should always be stated. In comment, LOURIE states that at the Brazzaville conference in 1948 it was ruled that the upper limits of cell count and total protein (Sicard and Cantaloube) for the lymphatico-blood stage of trypanosomiasis should be 3 cells per cmm. and 0·025 gm. protein per 100 cc.

VAUCEL and CECCALDI (p. 503) have found infection in patients (in West Africa) who had been treated for infections 5–12 years previously. They discuss the question whether these represented reinfections or reactivations after long latent periods, but without reaching definite conclusions.

Discussing the transitory neurological signs observed in sleeping sickness, GELFAND (p. 411) describes a case in which the symptoms suggested encephalitis or tuberculous meningitis, but trypanosomes were present in the cerebrospinal fluid and treatment with tryparsamide and pentamidine was successful in removing the cerebral symptoms.

Treatment and Drug Prophylaxis

SICÉ (p. 876) writes of some reactions experienced by a patient being treated with various drugs for sleeping sickness.

It has long been known that Suramin (Bayer 205) persists for considerable periods in the body, and that there is no particular tissue which acts as a storage depot. SPINKS (p. 772) has investigated the subject and has confirmed the high and persisting plasma levels. Closely related compounds also persisted, but therapeutic activity was not correlated with persistence. The possible hydrolytic products of Suramin were rapidly eliminated, so that it seems to resist hydrolysis in the body. The paper should be read in the original.

As a result of staining experiments at different hydrogen ion concentrations, SCHUELER (p. 313) concludes that when trypanosomes become drug-resistant there is a significant shift in the iso-electric points of the proteins.

HARVEY (p. 690) discusses the sulphydryl and disulphide group in relation to arsenic resistance of trypanosomes, but without finding a definite relationship which would explain the phenomenon. WILLIAMSON and LOURIE (p. 413) have confirmed the finding of van Hoof that melarsen oxide (which contains a melamine group) is active against arsenic-resistant trypanosomes. They discuss the mechanism of arsenic resistance, and the action of the melamine group in the combination of melarsen oxide (and other substances) with the trypanosomes, but their argument should be read in the original. TRINQUIER and PELLISSIER (p. 877) report favourably on a French equivalent of melarsen oxide given by mouth in sleeping sickness at Brazzaville, but the period of observation was short. In a second paper (p. 877) they also report favourably on melarsen administered by mouth. Details of dosage are given.

CECCALDI *et al.* (p. 771) have been disappointed with their results in treatment of *T. gambiense* infections with *p*-arsenosophenylbutyric acid.

NODENOT (p. 161) has analysed the results of treatment of sleeping sickness, in French West Africa, with pentamidine, and LOURIE has constructed from his text a table showing these results. In high dosage the drug is effective up to, but no later than, the time when the infection begins to involve the central nervous system. The author recommends intramuscular doses of 3 mgm. per

kgm. body weight, repeated daily or on alternate days for 5 doses; but he used bigger doses in some series. SALEUN and CHASSAIN (p. 875) have used pentamidine in French Equatorial Africa, intravenously in hospital but intramuscularly in the field, where intravenous administration to ambulant patients is regarded as too risky. Intravenous doses of 2 mgm. per kgm. each day for 8–10 days were rather too toxic, but with intramuscular administration even 3 mgm. per kgm. was not toxic. Pentamidine can be used in pregnancy. The results promise to be good, though the time of observation is short; there was a favourable effect in 26 cases which had proved refractory to other drugs. TRINQUIER and ARNOULT (p. 313) also write very favourably of the results obtained in French Equatorial Africa by the use of pentamidine in early *T. gambiense* infections. Cure may be effected within 10 days in early cases, but the drug is inadequate in late cases, though it may be useful in association with tryparsamide.

HARDING and HUTCHINSON (p. 410) write favourably of antrypol and (especially) pentamidine in prophylaxis; they think that general drug prophylaxis is more effective than treatment of cases in checking an epidemic. SALEUN and CHASSAIN (p. 878) in French Equatorial Africa report good results after a single intramuscular injection of 4–5 mgm. per kgm. pentamidine in prevention of infection, for a period of 6 to 8 months.

LAUNOY (p. 1071) gives figures displaying the curative and prophylactic effects of pentamidine given subcutaneously to rats, against several species of trypanosomes. Although LAUNOY and JEANPIERRE (p. 879) show that pentamidine given by mouth has little prophylactic action in rats against subsequent injection of *T. equiperdum*, LAUNOY (p. 1071) reports that an insoluble preparation of pentamidine, when given by mouth to rats, exerts a prophylactic action against subsequent intraperitoneal infection with *T. gambiense*.

VAN HOOF *et al.* (p. 412) show that in *T. gambiense* infections in the Belgian Congo, propamidine and pentamidine have similar protective and curative properties, but that propamidine is more toxic, giving rise to paresis in some cases. Nervous symptoms could be avoided if propamidine was given intramuscularly. EERAERTS (p. 412) has used propamidine as a prophylactic in the Belgian Congo, where he gave intramuscular doses up to 5 mgm. [presumably of the isethionate] per kgm. for adults. Two injections of the 4 per cent. solution were given at an interval of 6 months, and very good prophylaxis was reported. In the dose of 5 mgm. per kgm. propamidine shows a strong tendency to produce abortion in pregnant women.

Animal Trypanosomiasis

HOARE (p. 504) discusses the transmission of pathogenic trypanosomes of man and animals by biting flies other than *Glossina*, and shows that infection of domestic animals by *T. vivax* is a serious problem in some countries in which tsetse flies do not occur. He also discusses the possible relationship between *T. evansi* and *T. brucei*, and thinks it possible that the former may have arisen from the latter, or *vice versa*.

The chemotherapeutic activity of cinnoline derivatives for *T. congolense* infections is discussed by KENEFORD *et al.* (p. 690).

WILDE (p. 414) has shown that cattle can be kept in excellent condition in East Africa, in spite of infection with trypanosomes (excluding *T. brucei*) by regular prophylactic treatment with a phenanthridinium compound or with Stibophen. He gives details of the different dosage schedules he used in this work.

CULWICK and FAIRBAIRN (p. 313) have found *T. simiae* in two new hosts in East Africa—horse and cattle. They have measured these trypanosomes,

finding three forms, which they discuss in relation to their theory of syngamy in trypanosomes.

MARSHALL (p. 495) discusses the glucose metabolism of *T. evansi* in relation to the trypanocidal action of certain drugs, but the details should be sought in the original.

KLEINE (p. 689) discusses the control of surra in Russia and of animal trypanosomiasis in Africa.

BESSEMANS *et al.* (p. 587) have succeeded in infecting a mouse by injection of a single *T. equiperdum*, in one of 36 attempts. They failed with *T. gambiense*. Failure to infect was quite common even when 50–200 trypanosomes were injected.

The distribution and rate of metabolism of phosphorus compounds in *T. equiperdum* have been studied by MORACZEWSKI and KELSEY (p. 587), but for details the original abstract should be consulted.

HOPPE and CHAPMAN (p. 505) give their reasons for thinking that hypoglycaemia is the cause of death in albino rats infected with *T. equiperdum*. CHEN and MCCREARY (p. 505) have assayed on *T. equiperdum* the trypanocidal action of arsenical drugs by methods previously used for antimonials. Details should be sought in the original. CHEN and GEILING (p. 691) have been able to show that cysteine hydrochloride inhibits the effect of trivalent and pentavalent antimonials on the glucose metabolism of *T. equiperdum*. CHEN (p. 691) has also shown that it inhibits the effect of nitrogen mustard on glucose metabolism. He (p. 773) has investigated the inhibition of certain glycolytic enzymes of *T. equiperdum* by antimonials and arsenicals.

DODD (p. 52) shows that the compound Furacin has a fairly high degree of activity *in vivo* against *T. equiperdum*, and against various bacteria, when given as suspension by stomach tube. KRANTZ and EVANS (p. 52) demonstrated that this drug has only a low degree of toxicity.

ERCOLI and WILSON (p. 773) show that BAL not only interferes with the toxicity of ma harsen, but it also (and much more strongly) interferes with its therapeutic activity against *T. equiperdum*. A combination of the two substances, therefore, would not be suitable for treatment.

CALDWELL and GYÖRGY (p. 417) show that in rats maintained on a diet deficient in biotin, and infected with *T. lewisi*, there was intense and prolonged infection. The effect of biotin deficiency is probably to cause diminution in the production of ablastin and trypanolysin. TAYLOR and BECKER (p. 773) describe the liver changes observed in rats fed on a diet deficient in pantothenate, and infected with *T. lewisi*. Such rats develop very heavy infections.

Chagas's Disease

DIAS (p. 1072) gives a general account of Chagas's disease in South America.

Chagas's disease has been found in many of the municipal districts of Rio Grande do Sul, Brazil, and is carried by *Triatoma infestans*. PINTO (p. 53) discusses the clinical features of the disease as it is seen in this area. ROMÁN (p. 415) found up to 23 per cent. of people infected with *T. cruzi* in part of Bolivia where *T. infestans* was the only known vector. Infection was also present in some dogs and cats examined.

TOBIE and REES (p. 880) have grown *T. cruzi* in a dialysate medium. MEYER and XAVIER DE OLIVEIRA (p. 983) have cultivated *T. cruzi* in tissue culture, and have observed that the entire cycle takes place in one cell. The paper should be read in the original. An autoclaved medium, free from cells and coagulable protein, and in which *T. cruzi* can be cultivated, is described by DE FREITAS and DE CASTRO (p. 1073).

HAUSCHKA (p. 415) has compared the susceptibility of male and female mice to various strains of *T. cruzi*.

MUNIZ *et al.* (p. 55) attempted to immunize monkeys with killed cultures of *T. cruzi*, but without success.

MAZZOTTI (p. 163) found natural infection with *T. cruzi* in *Triatoma protracta woodi* and *T. gerstaeckeri* in Mexico. A new species, *Triatoma delpontei*, has been found infected with *T. cruzi* in nature, by ROMAÑA and ABALOS (p. 314).

DE FREITAS (p. 315) reviews the laboratory methods of diagnosis of Chagas's disease, which include xenodiagnosis, animal inoculation with blood from the patient, haemoculture, and the complement fixation test. He quotes a considerable amount of his own original work, and concludes that xenodiagnosis is the best diagnostic procedure, and that the complement fixation test is very useful; the other two procedures gave poor results. MUNIZ (p. 54) describes a precipitin reaction which is particularly valuable in the early stage of Chagas's disease before definite symptoms appear; it is not very useful in chronic cases.

PELLEGRINO and MESQUITA (p. 506) show that false positive reactions to the complement fixation test for *T. cruzi* infection may be given if sera are stored in the ice-chest before the test is performed, but that these false positive results can be avoided if the test is carried out on fresh specimens.

ROMAÑA and GI (p. 316) refer to artificial xenodiagnosis, the patient's blood being drawn into a tube which is then covered with animal skin. The bugs bite through this skin and take in the blood. The test is useful if for any reason it is impossible to have the patient bitten directly by the bug.

DEANE (p. 417) shows that Triatomid bugs are often found to be infected with *T. conorrhini*, which may lead to confusion in xenodiagnostic tests unless the flagellates are tested by injection into laboratory animals [which seems to be a most important fact].

MUNIZ and DE AZEVEDO (p. 416) report experiments which indicate that there is an allergic condition in the pathogenesis of Chagas's disease.

PONDÉ *et al.* (p. 314) have performed the xenodiagnostic test and a complement fixation test on certain patients passing through the cardiology department of a hospital in Bahia, Brazil; the patients showed signs or symptoms which suggested Chagas's disease, and this was confirmed by one or the other of these tests. The symptoms of cardiac disease associated with Chagas's disease are described. PONDÉ (p. 1074) found partial auriculo-ventricular block in 6 of 40 patients with Chagas's disease, and total block in 11. He describes other changes detected by electrocardiography in this series of cases. LARANJA *et al.* (p. 589) describe the electrocardiographic changes in Chagas's disease, and give details of the variations from normal which they observed. VALLS (p. 416) made an electrocardiographic study of a considerable number of patients proved to have Chagas's disease, having first excluded those with cardiac conditions due to other causes. Apart from a few cases of A-V block, the lesions found were slight, and there was little impairment. Most of the patients were young. ROMAÑA (p. 316) reports cases of chronic myocarditis and of encephalopathy due to Chagas's disease.

In Venezuela, PIFANO *et al.* (p. 1072) have cultivated *T. rangeli* from the blood of a girl suspected of Chagas's disease, and describe its characters.

Charles Wilcocks

MALARIA

PAMPANA, E. **Malaria in Europe 1938–1947.** *Epidemiological & Vital Statistics Rep. W.H.O.* 1948, Nov., v. 1, No. 18, 392–400. [Refs. in footnotes.] [In parallel French & English.]

This is an interesting summary of all available information regarding the incidence of malaria in all European countries except Russia during the decade

which included the war years. The information is inevitably very incomplete but sufficient to justify the conclusion that outbreaks of malaria attributable to war conditions were much less widespread and severe than those which followed the 1914–18 war. The end of World War II coincided with the introduction of DDT as a residual insecticide. It is justifiable to conclude that this contributed materially to a lower malaria incidence than could reasonably have been expected. *Norman White*

FISCHER, L. Einheimische Malaria und Anophelismus in der Nachkriegszeit. [**Indigenous Malaria and Anophelism in the Post-War Period.**] *Deut. med. Woch.* 1948, Nov. 5, v. 73, Nos. 41/42, 515–18, 3 figs. [24 refs.]

The article reviews briefly the past and present incidence of indigenous benign tertian malaria in Germany. In considering, with special reference to south Germany, the possibility of continued outbreaks the author discusses climatic factors, the habits and distribution of the *messeae* and *typicus* races of *Anopheles maculipennis*, the influx of gametocyte carriers, and the living conditions of the people under normal circumstances and as a result of the recent war. More importance is attached to *messeae* than to *typicus* as a potential vector. It is considered that limited foci of malaria may continue to occur where, as a result of the war, there is sufficiently increased contact between man and mosquitoes, but that mosquito destruction and amelioration of conditions should soon eliminate such outbreaks. *D. S. Bertram*

HOFFMANN, R. Ein Beitrag zur Geschichte, Klinik und Entomologie der Malaria in Oberschlesien. [**Malaria in Upper Silesia.**] *Öffentl. Gesundheitsdienst.* Leipzig. 1943, Apr., v. 9, Nos. 7/8, A 137–43, 2 figs. [10 refs.]

Malaria—or rather fever which almost certainly was malaria—has existed in this district since 1870, though cases then were very few. From 1880 onwards the numbers increased rapidly, " due to a large increase of small unimportant foci." In 1913 there were 100 cases reported; in 1917, 862 and during this period, 1913–17, there were 2,149 cases reported. In the Bielitz district, the infection is almost exclusively benign tertian; in Pless, malignant tertian has been found in several places and a few quartan infections. Clinically, the disease is usually mild; cachexia is rarely seen. The vector is *A. maculipennis* and nearly all *messeae*. Of 21 foci mentioned in which the mosquitoes were captured in byres, cellars and dwellings, in two the species is not stated, in one *A. m. typicus* alone was caught, in one *typicus* and *messeae*; in the other 17 *A. m. messeae* only. *H. Harold Scott*

KLOSE, F. & EISENTRAUT, M. Das Auftreten der Malaria in der Provinz Brandenburg im Jahre 1942. [**Malaria in Brandenburg Province in 1942.**] *Öffentl. Gesundheitsdienst.* Leipzig. 1943, Nov., v. 9, Nos. 21/22, A 325–9.

In 1942 malaria became prevalent among prisoners of war in Brandenburg Province. The prisoners treated numbered 5,595, of whom 2,213 were Jugoslavs, 1,815 French, 1,300 Russians and 267 British. Plasmoquine, 0·01 gm. thrice daily for three days after two days of atebrin [mepacrine], 0·1 gm. twice daily, were the drugs used and the results are stated to have been very good. Thus, among the Jugoslavs there were 355 cases between May and December 1941, but only 5 in the whole of 1942. During this year (1942) there were altogether only 109 cases: the 5 Jugoslavs just mentioned, 63 Russians, 34 British and 7 French.

Among German soldiers serving abroad, those in Russia suffered most; 6·6 per cent. in the northern theatres of war, 14·3 in the middle, 28·4 in the

southern and 14·1 per cent. in unspecified places at the front. Two-thirds were first attacks, one-third were relapses. It is said that only 82 cases altogether occurred among the non-military population: 10 Germans, 23 Russians, 17 Croats, 12 Jugoslavs, 8 Ukrainians, 4 Hungarians, 2 Bulgars and one each of Italian, Slovene, Dutch, Belgian, French and Spanish. A list is given of nearly a score of places in the Province where conditions favour the development of *Anopheles*. *H. Harold Scott*

REV. SANIDAD E HIG. PÚBLICA. 1946, Sept. & Nov., v. 20, Nos. 9 & 11, 917–69; 1114–77. Estadística de los Dispensarios Antipalúdicos dependientes de la Dirección General de Sanidad. [**Statistics of Antimalaria Dispensaries of the Central Health Administration.**]

These statistical tables concern cases of malaria, fresh infections, diagnosed in each of the antimalaria dispensaries in each of the Provinces of Spain during the years 1944–45 and 1945–46 (1st June to 31st May). Tables record the incidence in five age groups; the incidence of *P. vivax*, *P. falciparum* and *P. malariae* infections, and the monthly incidence of each species of infection. The total number of new infections recorded in Spain in 1944–45 was 163,994; in 1945–46, 89,847. Of the latter 84,838 were *P. vivax*, 4,894 *P. falciparum*, 60 *P. malariae* and 55 mixed infections. *Norman White*

JERACE, F. La malaria nell'Agro Romano nel quinquennio 1943–1947. [**Malaria in the Agro Romano 1943–47.**] *Riv. di Malariologia*. 1948, June, v. 27, No. 3, 103–10, 1 fig. & 4 graphs. English summary (9 lines).

This is a description of the severe epidemic of malaria that afflicted the Agro Romano in 1944. The Agro Romano is the territory that is subject to the administration of the Rome Municipality. It extends to and includes 48 kilometres of the coast line of the Tyrrhenian Sea and has a population of some 250,000. Malaria is endemic everywhere west of Rome, more particularly near the coast, but energetic measures before the war had brought the disease under control. In only two of the years between 1933 and 1943 inclusive did the annual notification of malaria cases exceed 2,000. In 1944, 9,063 cases were recorded of which 7,986 were primary infections: the highest monthly incidence was in August, 2,433. War damage, the suspension of malaria control measures, the immigration of troops many of whom were infected with malaria, the introduction of new strains of parasites, the scarcity of antimalaria remedies, and forced movements of the population were all important factors in contributing to the severity of the outbreak. In 1945, the total number of cases recorded rose to 11,025; of these, however, only 2,965 were primary infections. Thereafter there was rapid improvement. In 1947, only 495 cases were notified. During the first five months of 1948, only 78 cases were found: all of these were relapses and 45 were imported cases. DDT, which was first used in 1944, has contributed much to the noteworthy success of the control campaign.
Norman White

BALZAR, M. Il pericolo della malarioterapia practicata in zone con anofelismo. [**Danger of practising Malaria-Therapy in Anopheline-Infested Areas.**] *Riv. di Malariologia*. 1948, Apr., v. 27, No. 2, 65–70. English summary (7 lines).

In the Provincial Mental Hospital at Vercelli, the treatment of neurosyphilitic patients with malaria therapy was started in 1938, at first by inoculation of infected blood and later by mosquito transmission. Nothing untoward happened till 1943 when 33 cases of locally acquired *P. vivax* infection occurred among

the inmates and staff of the institution and 7 cases among the nearby inhabitants of Vercelli; in the two following years the numbers of primary infections were 53 and 8, and 131 and 12. The anopheline density in these years was probably much increased. The scarcity of food was such that rice cultivation was allowed close up to the inhabited parts of the town. The scarcity of materials and disorganization generally arising from the war prevented the application of prompt measures of control. In 1946, the hospital buildings were treated with DDT with, excellent results. In that year only four fresh infections were acquired in the hospital and only 6 in the vicinity. The author concludes that malaria therapy should not be practised in areas in which vector mosquitoes are prevalent unless supplies of DDT are available for the adequate disinfestation of at least the quarters in which the patients in question are housed.

Norman White

SCHWETZ, J. **Notes on Endemic and Acute Malaria in Central African Natives.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan., v. 42, No. 4, 403–8.

In endemic malaria areas in Central Africa, parasite rates are much higher among African children than among African adults. In children, *P. falciparum* dominates but *P. malariae* and even *P. vivax* infections occur, with gametocytes of all three species: in adults only trophozoites of *P. falciparum* are found, with occasional rare crescents. In hyperendemic areas, the peak of infection is reached at the age of 1 to 2; in hypoendemic areas at from 5 to 8 years. In the latter, the *P. malariae* infection rate is low and *P. vivax* is very rare.

In infants, congenital malaria has not been found: *P. falciparum* appears first, later *P. malariae* and last *P. vivax* infections.

In endemic areas, the diagnosis of fever of malarial origin may be difficult; the parasites may only be commensals. The microscopical blood picture can be a useful aid to differential diagnosis. In endemic malaria, large and more or less thick trophozoites in cells with specific alterations (deeper coppery colour, and Stephens-Maurer dots) are characteristic. In acute malaria, minute trophozoites are found which have not yet been able to cause alterations in the red cells.

In high plateaux of Central Africa, epidemic malaria sometimes occurs; in epidemic malaria adults and children are infected in like proportion and both groups may show parasites of *P. malariae* and even of *P. vivax*.

Norman White

HSU, Kuo-Chin. **Malaria in Southern and Western Szechuan with a Note on the Occurrence of** *Schistosomiasis japonicum*. *Chinese Med. J.* Shanghai. 1948, June, v. 66, No. 6, 319–23. [20 refs.]

This is a record of a journey made in the south-west part of Szechuan. In each of nine localities children under 12 years of age were examined; blood smears from all children with splenic enlargement were examined. Enquiries were made from local medical practitioners regarding the incidence of malaria. Collections were made of anopheline larvae.

Malaria was very prevalent in Suifu were a spleen index of 28·5 was recorded: in 1939 it was only 6·1 per cent. The movements of troops and refugees contributed to the increased prevalence which was specially marked after the completion of the aerodrome; *P. falciparum* infections became much more numerous. Of 1,189 positive blood smears, 68·6 per cent. contained *P. vivax*, 28·6 per cent. *P. falciparum* and 2·8 per cent. *P. malariae*.

A. hyrcanus var. *sinensis* was the most prevalent anopheline. It was found breeding in rice-fields, slowly moving streams, stagnant pools and in a variety

of collections of casual water. Other species found, in small numbers, were *A. minimus*, *A. pattoni*, *A. barbirostris* and *A. hyrcanus* var. *nigerrimus*.

The author found a boy suffering from *Schistosoma japonicum* infection. *Oncomelania* snails were found in many places. Ankylostomiasis was very prevalent. *Norman White*

MIYAO, I., TAKEI, H., HATORI, J. & NODA, H. **Investigative Studies concerning Malarial Infection among the Natives of Kainanto.** *Kitasato Arch. Exper. Med.* 1942, Aug., v. 19, No. 2, 73–84. [21 refs.]

HERNÁNDEZ LIRA, P. Algunos aspectos de la epidemiología del paludismo en el nordeste de la República Mexicana. [**Epidemiological Aspects of Malaria in the North-Eastern Part of Mexico.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Aug., v. 27, No. 8, 699–705. English summary.

This is a short description of a malaria control programme intended to cover an area of north-east Mexico, triangular in shape the points of which are the three towns Matamoros, Nuevo Laredo and Monterrey. Work has been started in Monterrey, an industrial city of 232,000 population. The Antimalaria Dispensary of Monterrey report that the average annual incidence of malaria cases during the last five years has been 550. The examination of 1,500 school children gave a spleen index of only 3 per cent. Malaria parasites, *P. vivax*, were found in only 1·9 per cent. of 2,000 films examined.

The more important breeding places of anophelines in the city are listed. Four species of *Anopheles* have been identified: *A. pseudopunctipennis*; *A. punctipennis*; *A. quadrimaculatus*; and *A. albimanus*. *A. pseudopunctipennis* is the most prevalent especially during the months June and July, and from September to November inclusive. A private company has undertaken considerable engineering work designed to eliminate mosquito breeding, and DDT has been used extensively. When the work in Monterrey is completed Matamoros will receive similar attention. *Norman White*

DUBIN, I. N. **A Search for Exoerythrocytic Forms in Human Malaria by means of Tissue Cultures of Bone Marrow.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 330–32.

"In a search for exoerythrocytic forms in human malaria, tissue cultures were made from the bone marrow of patients with sporozoite-induced infections, both in the pre-patent period as well as after development of parasitemia. This was done in *P. falciparum* infections in 6 instances and in *P. vivax* infections in 20 instances. No exoerythrocytic forms were seen in the cultures."

MACKERRAS, M. J. & ERCOLE, Q. N. **Observations on the Development of Human Malarial Parasites in the Mosquito. I. Morphological Changes.** *Australian J. Exper. Biol. & Med. Sci.* 1948, Sept., v. 26, Pt. 5, 439–47, 2 figs. & 1 coloured pl. [17 refs.]

This is an account of the development of *Plasmodium vivax* and *Plasmodium falciparum* of Melanesian strains in *Anopheles punctulatus punctulatus*.

The preparations for study were made from mosquitoes fed on gametocyte carriers and dissected at varying intervals after the blood meal. The preparations so obtained were air-dried and stained by Leishman's stain.

Material at late stages in the infection was examined in fresh preparations or after fixation and staining by various standard methods.

The events in sporogony are described on familiar lines and speculation is made as to whether the two masses of chromatin often seen in the female

gametocytes indicate meiotic division preliminary to fertilization or whether they are the male and female nuclei prior to fusion.

Development of the oökinete and the oöcysts on the outer surface of the gut wall is described, but no new facts are brought out. The growth of the oöcysts under similar conditions was said to be more rapid in the case of *P. vivax* than in that of *P. falciparum*, sporozoites entering the glands two or three days earlier in the case of the former parasite.

Infected mosquitoes kept for any length of time showed a steady depletion in sporozoite content even when they were fed on carbohydrate food only.

H. E. Shortt

MACKERRAS, M. J. & ERCOLE, Q. N. **Observations on the Development of Human Malarial Parasites in the Mosquito. II. Factors influencing Infection.** *Australian J. Exper. Biol. & Med. Sci.* 1948, Sept., v. 26, Pt. 5, 449–58, 2 figs.

An attempt is made to assess the influence of various factors on the infections produced in anophelines fed on gametocyte carriers of *Plasmodium vivax* and *P. falciparum*.

The probable number of gametocytes ingested by the mosquito is first considered and then the findings in each of the two species are considered separately.

P. vivax.—The results obtained in infecting mosquitoes were often contradictory and no factor relative to either insect or plasmodium could be demonstrated as the cause of greater or lesser infection rates in the mosquito.

P. falciparum.—Here, again, equivocal results seem to have been obtained and the curious inference is drawn that immature gametocytes can produce oöcysts but that these do not develop normally as will be evident from the following quotation—" these gametocytes were of the usual crescentic shape, but many were apparently immature as large numbers of the cysts which formed died before reaching maturity and the sporozoite rate of the batch was only 42 per cent."

The case of one patient is described where gametocytes of *P. falciparum* consistently failed to infect mosquitoes and this is put down to " some inherent functional peculiarity, the cause of which is quite obscure." [There would appear to be at least the possibility that some other less obscure cause was operating, such as the surreptitious use of paludrine.]

The causes responsible for reduction of viable gametocytes in the first 24 hours after the mosquitoes' blood meal are considered, such as the well-known phenomenon of phagocytosis. The description is given of one batch of mosquitoes which were fed on a *P. vivax* gametocyte carrier in which the mosquitoes showed numerous minute brown spots on the gut wall. These are interpreted as representing the points of penetration of the gut wall by vermicules which, later, failed to form oöcysts [this seems improbable].

H. E. Shortt

SAUNDERS, G. M., TALMAGE, D. W. & SCOTT, V. **The Use of *Plasmodium vivax* preserved by Freezing in Inducing Malaria.** *J. Lab. & Clin. Med.* 1948, Dec., v. 33, No. 12, 1579–87.

The therapeutic use of malaria continues to be so widely practised that any easy method of maintaining a strain over long periods without the use of human subjects would be of great advantage.

It was for this reason that the method here described was worked out and tested. Blood from malarial donors was collected and prevented from clotting

either by mixing five volumes of blood with one volume of 4 per cent. sodium citrate, or by defibrinization.

The blood was next transferred to thin-walled glass ampoules in two to four ml. amounts and these were sealed in a flame. The contents were next rapidly frozen by immersion of the ampoules in a freezing mixture of ethyl alcohol and dry ice at −70° to −80°C. By rotating the ampoules individually freezing was complete in a few seconds and the ampoules were then stored in dry ice at −70°C. For use, the ampoules were rapidly thawed at the bedside by immersion in a water bath at 40°C. and the contents immediately inoculated intravenously, two or three ampoules being used for one inoculation.

Results.—Successful transmission of malaria was obtained after more than five months storage of blood and the overall success rate in 46 subjects was 87 per cent. [40 subjects]. The possible causes for the failures are discussed, such as previous malarial infection, race, inadvertent use of antimalarial drugs, the stage of the malarial parasites when frozen, and other factors.

There was no significant difference in the results obtained with defibrinated and citrated blood, nor did the length of storage appear to affect the results.

The average incubation period was 12·4 days, somewhat longer than after direct transfers of blood but the clinical course of the resulting malarial infection differs in no way. The preservation technique caused haemolysis of the red cells, thus freeing the parasites, which showed poor staining reactions but no untoward results attributable to the inoculations were seen in patients.

H. E. Shortt

MACKERRAS, M. J. & ERCOLE, Q. N. **Observations on the Life-Cycle of** *Plasmodium malariae. Australian J. Exper. Biol. & Med. Sci.* 1948, Nov., v. 26, Pt. 6, 515–19, 3 figs.

Although quartan malaria is widely distributed throughout the tropics, much less is known about its life history than that of the other malaria parasites. Melanesian strains in particular have been little investigated and this paper remedies the defect to a small extent. A number of *Anopheles punctulatus punctulatus* were allowed to feed on a carrier of *P. malariae* gametocytes in New Guinea and were then sent to Cairns, Australia, where they were kept at 73°F. Oöcysts, 25μ in diameter, were present on the 16th day. These cysts showed the typical distribution of fine black pigment in double lines. A light infection of sporozoites reached the glands by the 31st day or slightly earlier. At this same temperature, *P. vivax* takes 15 to 16 days and *P. falciparum* 18 to 20 days.

Five mosquitoes of this batch were still alive on the 24th day and for the next 10 days they were given an opportunity to feed on a volunteer who actually received 11 bites during this time. Three of the five mosquitoes harboured sporozoites. Parasites were first seen in the man's blood 24 days after the first bite ; symptoms of the disease started a fortnight later still. Two other volunteers received inoculations of blood containing the infection. All three cases were mild and the parasitaemia did not exceed 2,300 per cmm. Gametocytes were first seen 23 days after the appearance of trophozoites ; they were never numerous and they proved uninfective to mosquitoes.

The morphology of the parasites was studied in one of the two blood-infected volunteers who exhibited a typical quartan fever. By 24 hours the parasites contained pigment and were " amoeboid " in shape. By 48 hours the trophozoite almost filled the blood cell and division of the chromatin had started. By the 64th hour, division of the chromatin was completed and the pigment had aggregated. Merozoites numbered 5–10 the average being 8.

[It will be noted that this Melanesian strain shows few differences from the classical form.]

P. C. C. Garnham

GAUD, J. Rythmes saisonniers d'activité d'*A. maculipennis* et d'*A. claviger* au Maroc en fonction de l'altitude. [**Seasonal Breeding of** *Anopheles maculipennis* **in Morocco in relation to Altitude.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 7/8, 494–8, 1 map & 1 graph.

The behaviour of *A. claviger* and *A. maculipennis* var. *labranchiae* was compared in the plains and mountains of Morocco. The latter species constituted more than 80 per cent. of the total anopheline population and is the principal vector of malaria. Both species breed in slowly running water, rich in vegetation; in fact the same breeding places are used by the two mosquitoes. In the mountains, *A. claviger* is first found alone, then the two are found together during the hot season and later *A. maculipennis* disappears. Below 500 m. development of *A. maculipennis* continues throughout the year ; at 1,000 m. it is found only for six months, and above 1,500 m. only for four months. The breeding of *A. claviger* is also influenced by altitude, its upper limit is well above 2,000 m. and its lower limit in the summer months is about 1,000 m. The author suggests differential control by larvicidal measures as opposed to permanent works, based on these observations. *P. C. C. Garnham*

TAKEI, H. **Experimental Studies concerning the Growth of Anopheles in Sea Water in Kainanto.** *Kitasato Arch. Exper. Med.* 1942, Aug., v. 19, No. 2, 103–8.

" 1. We observed the growth of anopheles larvae in sea water.

" 2. Many species of anopheles are found in the southern district of Kainanto, but only *A. vagus* hatched."

ROBERTS, J. I. **A Parasitological Survey of African School Children in Nairobi Schools with Haematological Results of Malarial Infections.** *J. Trop. Med. & Hyg.* 1949, Feb., v. 52, No. 2, 31–3.

A survey was carried out on African school children living in Nairobi, Kenya, who belonged to several tribes. The results are given in four tables. About a quarter of the children showed malaria parasites in their blood and three-quarters had intestinal helminths. The malaria was chiefly caused by *P. falciparum*, though *P. malariae* (4 per cent.) and *P. vivax* (0·28 per cent.) were occasionally seen. Helminths included species of *Ascaris*, *Ancylostoma*, *Taenia* and *Schistosoma* in that order of prevalence. *Entamoeba histolytica* was found in 5 per cent. of the children.

Fifty children suffering from malaria were investigated haematologically. The average red blood count was 2,650,000 per cmm., the haemoglobin, 8·84 gm., and the total white cells were 19,000 per cmm. including 22 per cent. pigmented forms. It is stated that the diet of these children was comparatively poor in the haemoglobin-producing element. *P. C. C. Garnham*

ROBERTS, J. I. **A Comparison of Haematological Results in Europeans and Africans suffering from Active Malaria.** *J. Trop. Med. & Hyg.* 1948, Nov., v. 51, No. 11, 228–34.

A study was made of the effect of malaria on the blood of patients during an epidemic of the disease in the town of Nairobi, Kenya Colony : 200 Africans and 100 Europeans were observed and an attempt was made to assess the degree of disability arising from the anaemia caused by the infections. The malaria was chiefly due to *P. falciparum* and medium or light infections were commonest (in four-fifths of both the European and African groups). The author states, however, that the numerical prevalence of parasites is no guide to the severity

of the case; even in cerebral malaria the peripheral blood and brain often harbour few parasites. [No evidence for this oft repeated statement is provided.] The anaemia was measured by the amount of haemoglobin (by the Hellige acid-haematin haemometer) and by the number of red blood corpuscles.

Normal figures [see also Haematology, below] for males at the altitude of Nairobi (5,500 ft.) are stated to be between 18·7 to 21·25 gm. per cent. haemoglobin and 5½ and 6½ million red blood cells. African cases of malaria gave an average percentage of haemoglobin of 11·56 gm. and 3,387,000 erythrocytes; Europeans, 13·09 gm. haemoglobin and 3,860,000 erythrocytes. The two races differed in the number of cases occurring within the normal haematological range, *viz.* 46 per cent. of Europeans but only 21·5 per cent. of the Africans. The two races differed also in other respects; pigmented leucocytes occurred in 22 per cent. of the Africans and in only 4 per cent. of the Europeans; immature blood cells were about four times as common in Africans; the white blood count was significantly higher in Africans (about 13,000 as compared with 8,000) and included many myelocytes. The mononuclear count was found to be little guide to the diagnosis of malaria; in normal Africans, it was found to be 6 per cent., in cases of malaria 8 per cent. with very wide variations.

[The author concludes that an appreciable degree of disability arises from the malarial infections, even though the parasitaemia was low. Two queries suggest themselves: was malaria the only cause of the anaemia, and how permanent were the effects?]

P. C. C. Garnham

MASSIAS, C. & HAO, N. D. La cirrhose atrophique du foie paludéenne. [**Atrophic Cirrhosis of the Liver in Malaria.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1948, Nos. 24/25, 826–30. [26 refs.]

The authors observed many cases of ascites in highly malarious areas of French Indochina. The clinical picture was that of Laennec's cirrhosis associated with pronounced cachexia and often with well-developed collateral circulation. Autopsies were carried out in some cases and disclosed small hard brown or yellow livers, the dominant lesion in which was annular sclerosis dividing the parenchyma into islands of cells which showed signs of degeneration or hyperplasia or both.

The authors consider that malaria was an aetiological factor of importance in the pathogenesis of the liver lesions. This opinion is based on the exclusion of certain other possible aetiological agents, including alcohol. The authors admit, however, that many other factors, such as nutritional status, may be equally involved.

An unconvincing survey of literature on the subject is given.

B. G. Maegraith

MOHAPATRA, G. S. **Cerebral Symptoms in Benign Tertian Infection.** *Indian Med. Gaz.* 1948, Sept., v. 83, No. 9, 412–13.

This note refers to a Hindu child of 4 years who was admitted to hospital suffering from a daily pyrexia and rigor, spastic paralysis and aphasia. The spleen was enlarged and palpable. The blood showed 65 per cent. haemoglobin and 3,380,000 erythrocytes per cmm.

At the height of the fever on the first afternoon and also on the next day, benign tertian malaria parasites were found in the blood: careful and repeated examination failed to show subtertian parasites.

The child reacted promptly to intramuscular quinine (after two days on alkalis only, so that the blood slides could be studied). The afternoon fever and rigor stopped on the fourth day and that night the child spoke a few words; and spoke freely next morning. Oral quinine was continued: the child could

walk on the seventh day, and movement was complete, with normal reflexes, a day or two later. The child was removed from hospital on the tenth day and was " keeping fit with usual physical and mental growth " several months later.

The author concludes that this case presents " positive evidence of the benign tertian parasite infecting the brain." [The author states that the duration of the " daily afternoon rise of temperature with rigor and fever " was 20 days : and later, that these features stopped (after treatment) on the fourth day. A more cautious conclusion in all the circumstances would perhaps be that a child suffering from malaria, with *P. vivax* in the blood and associated with central nervous manifestations, responded promptly to anti-malarial treatment. In a footnote, the Editor of the *Indian Med. Gaz.* refers to the difficulty at times of detecting subtertian parasites in mixed infections.]

H. J. O'D. Burke-Gaffney

CHUNG, Huei-lan, LIM, K. T., CHANG, A., WANG, W. P. & KOEH, Z. S. **A Case of Congenital Malaria occurring Seven Days after Elective Cesarean Section.** *Chinese Med. J.* 1948, Aug., v. 66, No. 8, 449–51. [22 refs.]

" A case of congenital malaria is reported. The child's mother was given a transfusion of blood from her brother who had tertian malaria three years previously. Eleven days later the mother underwent a cesarean section delivering a full term normal baby. On the next day, the woman developed chills and fever which recurred 48 hours later. *Plasmodium vivax* was found in the blood during the third paroxysm of chills and fever. The baby developed an irregular low fever on the seventh day and *Plasmodium vivax* was also recovered from its blood."

RAO, T. M. **M. T. Malaria simulating Acute Abdomen.** *Indian Med. Gaz.* 1948, Oct., v. 83, No. 10, 464–5.

Report of a case.

AUBRY, LAFFARGUE & PORTIER. Hépatisation grise suraiguë au décours d'un accès pernicieux palustre. [**Grey Hepatization as a Sequel of an Attack of Malignant Malaria.**] *Algérie Méd.* 1948, Aug.–Sept., No. 7, 407–10.

Report of a case.

BALDI, A. & DEL GIUDICE, V. Sui vantaggi delle dosi iniziali alte nella terapia con acridinici. (Studio comparativo.) [**Advantages of High Initial Doses in Treatment of Malaria with Acridine Derivatives.**] *Riv. di Malariologia.* 1948, June, v. 27, No. 3, 111–22, 2 figs. English summary (3 lines).

In Rome as elsewhere the posology of mepacrine and similar acridine derivatives in the treatment of acute malaria has changed considerably. In 1943–44, it was usual to administer 0·3 gm. a day for 7 days. In 1946–47, the practice was to give 1·5 to 1·6 gm. a day for the first 3 days and 0·3 gm. a day for the following 4 days. The cases in 1945 were mostly treated with the higher doses. To assess the advantage of the higher initial doses, the authors extracted 750 case cards from the records of the Institute of Malariology for the three years, 500 cases of *P. vivax* and 250 of *P. falciparum* infections. The cases are further subdivided into primary infections and relapses. Tables indicate the percentage of patients in the four groups that were free from fever and without parasites in the peripheral blood on each of the first five days of treatment. These tables show the much greater efficacy of treatment with the large initial doses of the drug.

Norman White

PATEL, S. R.; NARGUND, K. S.; KSHATRIYA, K. C. **Acridine Derivatives as Antimalarials. Part I. 5-amino derivatives of 3-7 dimethoxy acridine. Part II. 5-amino derivatives of 3-7-dimethoxy-6-chloro and 3-7-dimethoxy-8-chloro acridine** [PATEL & NARGUND]. **Part III. 5-amino derivatives of 7-methoxy-2-8-dichloro and 7-methoxy-2-6-dichloro acridine. Part IV. 5-amino derivatives of 7-methoxy-8-chloro acridine. Part V. Derivatives of 2-8-dichloro acridine** [KSHATRIYA & NARGUND]. *J. Univ. of Bombay.* 1948, Nov., v. 17, Pt. 3, 13–24, 2 figs.

HALAWANI, A., BAZ, I. & MORCOS, F. **Field Trials with New Antimalarial Drugs in Egypt.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 304–11. [19 refs.]

Ambulatory patients suffering from malaria were treated with one or other of the following compounds:—chloroquine, nivaquine C, camoquine, or paludrine, with a view to determining their value in the field. The camoquine course consisted of two doses, each of 0·25 gm., at an interval of twelve hours, so lasted only one day; the chloroquine course lasted 48 hours, and totalled 2·5 gm.; the nivaquine C course lasted 5 days, the total amount of drug being 1·8 gm.; and the paludrine course lasted 10 days, totalling 3 gm. of the drug. In addition to malaria infections most of these patients harboured heavy infections with hookworms, roundworms [*Ascaris*] and schistosomes. Over 400 patients in all were treated, and the drugs were all found rapidly to free the blood of *P. vivax* and *P. falciparum* parasites; paludrine was the least speedy of the four in this respect. Paludrine and nivaquine C, in the dosages employed, gave rise to no side effects; chloroquine gave rise to occasional vomiting and headache; and camoquine caused headache, giddiness and palpitation, nausea and vomiting, diarrhoea and abdominal pains, in some cases. The recurrence of parasitaemia within an observation period of six months was lowest in incidence among those treated with paludrine.

A. R. D. Adams

APARICIO GARRIDO, J. & BENITEZ CALVO, L. A. La cloroquina en el tratamiento del paludismo. Acción del medicamento sobre la sintomatologia y la parasitemia. [**Chloroquine in the Treatment of Malaria.**] *Med. Colonial.* Madrid. 1949, Feb. 1, v. 13, No. 2, 66–82, 12 graphs & 2 figs.

The English summary appended to the paper is as follows:—

"The authors report the results of the treatment of the tertian fever with chloroquina, used for the first time in Spain. A group of 12 persons (7 with induced paludism and 5 with natural paludism) were submitted to the treatment. They employed the doses and observed the rules given by 'The Board for Coordination of Malarial Studies' (a world spread organization of health). The fever disappears within 24 hours and sometimes it was possible to extinguish the access in evolution. The parasitemia also disappears within 24 hours in most of the treated persons and always within 48 hours. There were no poisoning nor secondary effects to be seen."

PACHECO, O., URCUYO G. F., GONZÁLEZ, A., JIMÉNEZ, A., BUTTS, D. C. A. & HERNÁN PÁEZ, L. Informe preliminar de un ensayo con el nuevo antimalárico S.N.7618. [**Preliminary Note on Trials with the New Antimalarial Drug SN 7618.**] *Rev. Med. Costa Rica.* 1946, July–Dec., v. 7, Nos. 147/152, 118–21.

The following is a translation of the authors' summary:—

In 39 cases of *Plasmodium vivax* and *P. falciparum* malaria studied, 36 were cured in less than 7 days. The other 3, although clinically cured, still showed gametocytes in the peripheral blood and all three were *P. falciparum*.

The average time of disappearance of the acute attack was 29·14 hours for *vivax* and 31·2 hours for *falciparum* infections.

The *vivax* gametocytes disappeared in all the cases noted. They were present originally in 7 cases.

The *falciparum* gametocytes disappeared in only one of 4 treated cases in which they were present.

There were no cases of severe intolerance to the drug requiring suspension of treatment. *H. J. O'D. Burke-Gaffney*

LOZANO MORALES, A. La terapéutica del paludismo por la metoquina. [**Treatment of Malaria with Metoquina.**] *Rev. Sanidad e Hig. Pública.* 1946, Nov., v. 20, No. 11, 1106–11.

This is a report of the treatment of 58 patients suffering from *P. vivax* infections with Metoquina (prepared in the Winthrop Laboratories, New York). The duration of the treatment was 5 days. The dose for patients 9 years of age and over was 0·3 gm. (3 tablets) a day. Parasites disappeared from the peripheral blood within 36 hours, average ; maximum 48 hours. All patients were free from fever on the third day of treatment. Thirteen of the 58 patients had relapses ; there was no relapse within 30 days of the end of treatment. It is concluded that metoquina is very effective in the treatment of infections with Spanish strains of *P. vivax.* *Norman White*

SANDICCHI, G. Relazione sugli esperimenti di terapia della malaria con il prodotto "Palusil". [**Treatment of Malaria with "Palusil".**] *Riv. di Malariologia.* 1948, June, v. 27, No. 3, 123–9. English summary (6 lines).

Palusil is the name given to Italian-made paludrine. Nine patients with *P. vivax* and 2 with *P. falciparum* infections were treated with this drug in the Institute of Malariology, Rome. The conclusion is reached that palusil is at least as effective as the acridine derivatives and as quinine in the treatment of malaria. *Norman White*

PATEL, J. C. & MEHTA, J. M. **Clinical Trials of "Cam-Aqi" in Malaria.** *Indian J. Med. Sci.* 1948, Nov., v. 2, No. 11, 675–9.

This paper reports the treatment with CAM-AQI of 36 patients suffering from malaria in Bombay. Nine had *P. falciparum*, 22 *P. vivax* and 5 had mixed infections. Some patients received 50 mgm. every 12 hours for 48 hours, five doses in all ; others received a single dose of 250 mgm. The average duration of fever was 55·9 hours after the commencement of the divided dose treatment, and 32·2 hours after the administration of the single dose. Asexual parasites disappeared from the blood within 62 hours (average) in both forms of treatment. The drug appeared to have no action on gametocytes. Twenty patients were observed for 4 months ; five of these had relapses after afebrile periods ranging from 11 to 45 days, average 31 days.

[For information regarding the chemical composition of CAM-AQI and other clinical trials see this *Bulletin*, 1948, v. 45, 39, and 1947, v. 44, 698.]

Norman White

MEIN, R. M. & ROSADO, P. N. S. Experiência com novos medicamentos contra a malária no programa da Amazônia. [**Experiments with New Antimalarial Drugs in Amazonia.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1948, May, v. 1, No. 4, 1059–1091, 2 charts. English summary.

Fifty-four patients suffering from malaria were treated with CAM-AQI ; 20 with chloroquine ; 7 with paludrine, and 15 with oxychloroquine. All four

drugs were effective in controlling the clinical symptoms of both *P. vivax* and *P. falciparum* malaria. In *P. falciparum* infections, chloroquine and paludrine failed to free the peripheral blood of parasites in a very large majority of the cases treated with them. CAM-AQI was considered to be the most effective drug of the four : it caused more rapid disappearance of fever and parasites in *P. vivax* infections than did the other three drugs ; it is effective against both *P. falciparum* and *P. vivax* infections ; a single dose is sufficient to rid the blood of parasites in both types of infection ; there are no contra-indications to its use. *Norman White*

HALL, D. Muriel & TURNER, E. E. **Structure and Antimalarial Activity. Part III. Some Benziminazoles.** *J. Chem. Soc.* 1948, Nov., 1909–11.

HUMPHLETT, W. J., WEISS, M. J. & HAUSER, C. R. **Preparation of Ketones from γ-Diethylaminobutyronitrile and Aromatic Grignard Reagents and their Conversion to Diamines. Synthesis of Quinacrine Analogs.** *J. Amer. Chem. Soc.* 1948, Dec., v. 70, No. 12, 4020–23.

COVELL, G., NICOL, W. D., SHUTE, P. G. & MARYON, M. **Studies on a West African Strain of *Plasmodium falciparum*. The Efficacy of Paludrine (Proguanil) as a Prophylactic Agent.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan., v. 42, No. 4, 341–6.

Attempts have been made at Horton at various times, without success, to infect indigenous forms of *A. maculipennis* var. *atroparvus* with strains of *P. falciparum* from India, E. and W. Africa, but success was achieved with strains of the same parasite from Sardinia and the Roman Compagna. Recently large numbers of the same species of mosquito were transported to W. Africa by air and allowed to feed on children with gametocytes of *P. falciparum* in their blood, but could not be infected. Defibrinated blood from a naturally infected child in Lagos was brought back on this trip and maintained in patients by blood inoculation. *A. stephensi* obtained from India, a common malaria carrier there and in the Persian Gulf, was found to be an efficient vector of the Lagos strain of *P. falciparum* and was used in the prophylactic experiments described in this investigation.

Four groups of 5 neuro-syphilitic patients infected 9 or more years previously were used in the paludrine tests. Each was infected once weekly for 6 weeks by mosquito-bite or by intravenous injection of sporozoites. Treatment with the drug was begun 3 days prior to infection and was continued for 6 days after the last infection. One group received 100 mgm. of the drug daily and a second group half this amount. A third group was given 100 mgm. twice weekly and a fourth 300 mgm. once weekly. None developed overt malaria during the whole course of the experiment and 18 of them inoculated later with sporozoites of the same strain proved to be susceptible. Three members of the staff were frequently bitten by infected mosquitoes during the experiment while taking 200 mgm. of paludrine twice a week and did not experience malarial attacks. Two others while in Nigeria were inoculated intravenously with a salivary gland suspension of a heavily infected mosquito, presumably carrying *P. falciparum*. They had taken paludrine daily in 100 mgm. doses for some days up to and including that prior to the inoculation and did not become infected. One patient infected like those in the other groups was treated at the same time with 5 grains of quinine hydrochloride daily and another with double this amount. In both cases malarial attacks were suppressed during treatment but both suffered attacks within 2 weeks after it

ended. A group of 5 similar patients infected in the same way served as controls and received no drug treatment. All had overt malaria within 14 days. The following is the authors' final observation :—

" Although paludrine acted as a true causal prophylactic of the Lagos strain of *P. falciparum* in each of the regimes under trial, it is considered that non-immune persons residing in or visiting West Africa should be advised to take not less than mg. 100 of the drug daily for the prophylaxis of malaria. For semi-immune subjects, such as native labour forces and locally recruited Government employees, a weekly dose of paludrine mg. 300 is recommended."

J. D. Fulton

D'AMBRA, G. B. Tecnica della profilassi antianofelica in Italia. [**Anti-Anopheline Control Measures in Italy.**] *Riv. di Malariologia.* 1948, Apr., v. 27, No. 2, 71–82. English summary (9 lines).

The author passes in review the antimalaria measures that have contributed to the effective control of the disease in Italy in the past. These have not all outgrown their usefulness. The use of DDT has engendered rather too much optimism as regards the ultimate complete eradication of malaria, by its use alone. DDT is of the greatest value in attacking epidemic malaria, but when dealing with endemic conditions a tightening up of older methods of control with a reorganization of the malaria control service will still be indispensable.

Norman White

SHOUSHA, A. T. **Species-Eradication. The Eradication of** *Anopheles gambiae* **from Upper Egypt 1942-1945.** *Bull. World Health Organization.* 1948, v. 1, No. 2, 309–52. 26 figs. (16 on 4 pls., 3 maps).

Anopheles gambiae entered Egypt from the Sudan at some time before March 1942, having probably been conveyed there in boats on the Nile. In that year dramatic outbreaks of malaria occurred first near the Sudan frontier, then at Asswan, and later as far north as Assiut. Enquiry showed that these were associated with a prevalence of *A. gambiae* which had not previously been reported in the country. Breeding places were numerous, particularly in the areas of perennial irrigation though its extent was largely controlled by low temperatures in the winter. In the hot season, low humidity probably shortened the average duration of life of the mosquito sufficiently to prevent active transmission for a large part of the year, the epidemics occurring during the limited season when breeding conditions, temperature and humidity were all favourable.

With the help of the International Health Division of the Rockefeller Foundation, a " Gambiae Eradication Service " was set up on the lines of the equivalent organization which had eradicated the same anopheline from Brazil a few years previously. The system of eradication used was one of organization and not of any special entomological technique. The basis of the organization was the *darak* or zone, an area of land in which two men working together could treat all water surface with hand-distributed one-per-cent. paris green in dust once a week. The boundaries of these zones, 641 in number, were very carefully defined so that they were readily identifiable on the ground as well as on the map. The two men in charge of the basic zone had no other duty than the distribution of paris green which they did on an organized schedule which could be readily checked. Five such zones were grouped into one " district " in charge of a foreman, a variable number of these into a " post " with a doctor or engineer in charge, and several of these in turn into a " division " each of which operated direct under the Field Headquarters with its supervising staff and laboratory.

A clear channel for the delegation of responsibility and the transmission of reports was thus provided. Each authority above the basic zone had an inspecting staff the duties of which included checking the anti-larval work and search for adult anophelines, though in pursuance of the policy of " one man, one job " these were carried out by different people. The results of this double check passed through each of the superior organizations which automatically sent inspecting staff to check negative records. By this emphasis on the importance of negative records with supporting data on the amount of searching which had preceded them, a reliable picture could be maintained at the central office where the campaign was directed. Traffic through the boundaries of the eradication zone was disinfested ; DDT, then difficult to get, was used on trains and pyrethrum on other vehicles. A therapeutic service was also instituted and in some cases houses were sprayed with pyrethrum to terminate local epidemic conditions.

Work was first started in February 1944. The last specimen of *A. gambiae* recorded was caught in February 1945, but work was continued till the following August and then stopped just before the time of year most favourable to the mosquito. In the following three months, 1,200 men were engaged in survey work examining 400,000 units of breeding area and 60,000 houses each week but no *A. gambiae* were found and eradication was considered complete. Other anophelines were not eradicated (this had not been attempted), and showed a normal seasonal rise.

The campaign is modestly contrasted with that in Brazil and the point is made that conditions in Egypt are less suited to this mosquito than those in Brazil on account of the lower winter temperatures which helped the control work by restricting breeding. In a brief study of past history, it is pointed out that previous epidemics of malaria in this part of Egypt, which have been attributed to an unrecognized prevalence of *A. gambiae*, are explicable on other and simpler grounds. [Without attributing previous epidemics to this anopheline, it would seem rational on the analogy of known happenings in Brazil to suggest that the actual primary invasion of Egypt took place some years before 1942 and that a " silent period " intervened between the invasion and the epidemics.]

The work described in this paper is truly of major importance, being only the second example of anopheline eradication in the world. It should be consulted in the original by all interested in the formation of national policies of malaria control. *G. Macdonald*

THOMSON, R. C. Muirhead. **D.D.T. and " Gammexane " as Residual Insecticides against *Anopheles gambiae* in African Houses.** *Nature.* 1949, Jan. 15, 109–10.

In experiments conducted in West Africa the author had drawn attention to the irritant effect of DDT-treated surfaces as a factor of such importance as to throw doubts on the value of house treatment with DDT as a control measure against *A. gambiae* [this *Bulletin*, 1948, v. 45, 405].

With the use of similar entomological methods, the experiments have been repeated in Dar-es-Salaam, Tanganyika, the DDT in kerosene used in W. Africa being replaced by DDT dispersible powder (1 lb. to 1 gallon of water). Large numbers of blood-fed *A. gambiae* were found in the window-trap daily, the number of dead anopheles on the floor being only a fraction of those which were escaping unharmed *via* the window-trap. " For at least two months after treatment not a single resting anopheles was found inside the hut, creating the familiar illusion that a high kill of mosquitoes had been obtained."

These experiments were repeated, substituting Gammexane dispersible powder P.530 [now replaced by P.520] for the DDT powder. In contrast to the experience with DDT, not a single living anopheles was taken in the window-trap up to thirteen weeks after treatment, numbers of dead *A. gambiae* being collected daily from the floor ; the latter lethal action continued for at least three months after treatment. There was no indication of that irritation which drives *A. gambiae* out of DDT-treated houses ; feeding took place inside the Gammexane-treated hut, but a high proportion of *A. gambiae* were killed before they could bite, especially in the first two or three weeks after treatment. The author emphasizes that these experiments were carried out under ideal conditions for testing an insecticide and that every possible resting place was heavily treated. The Gammexane powder was applied at the rate of 400 mgm. per sq. ft. (24 mgm. gamma isomer per sq. ft.) in a mixture of 1 lb. of P.530 in 1 gallon of water.

[The inference from Dr. Thomson's careful work is that Gammexane is effective in killing *A. gambiae* which enter dwellings for a blood-feed, whereas DDT is not. The broader aspect of the effect of this method, as a sole measure of control, on malaria incidence remains to be proved ; the prospects are promising.]

R. Ford Tredre

GEBERT, S. **Notes on certain Aspects of the Action of DDT Residual Sprays, and on the Partial Treatment of Dwellings as a means of Anti-Anopheline Protection.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Nov., v. 42, No. 3, 295–7.

In houses in an area of 16 square miles in Mauritius, the author collected 12,056 anophelines, mostly *Anopheles funestus*. The houses were then sprayed with residual DDT, but no dead mosquitoes were found in daily searches for three or four months afterwards. The author assumes that the mosquitoes were aware of the DDT in the houses and did not enter them. He supports this assumption with a theory that micro waves are emitted from the DDT which the mosquitoes can detect by their antennae !

He then gives figures to show that mosquitoes were present in 40 huts in another settlement. The walls of four of these huts were partially sprayed with DDT and an untreated hut was regarded as a "control". No mosquitoes were obtained in the four treated huts when they were searched 10, 36 and 50 days after treatment, but some mosquitoes could still be collected from the control hut.

[Publication of the facts might perhaps be justified, though as presented they are lacking in detail : the conclusions drawn from them are unwarranted.]

P. A. Buxton

ANDREWS, J. M. & GILBERTSON, W. E. **Blueprint for Malaria Eradication in the United States.** *J. National Malaria Soc.* 1948, Sept., v. 7, No. 3, 167–70.

Under the original proposal of Dr. Louis Williams it has been decided to try to eradicate malaria from the United States. The procedure decided on is a combined attack on the parasite and on the mosquito and the necessary inter-State and central organization has been set up for this purpose, including arrangements for standardized training. In endemic areas, DDT emulsion is applied twice a year to houses and other shelters at a dosage of 200 mgm. per sq. ft. (7 oz. per 1,000 sq. ft.). An effort is being made simultaneously to improve the diagnosis and notification of malaria cases and to ensure their

proper treatment with effective drugs, and in a few specially selected areas which were previously hyperendemic studies will be made of the intimate epidemiology of the disease and the conditions which may lead to its recrudescence.

After one year of work the programme has been put into operation in 80 per cent. of the 400 most malarious counties. Although the prospects are thought to be bright, permanent surveillance by specialized staff will be needed to detect recurrence. *G. Macdonald*

LENERT, Louva G. & LEGWEN, W. A. **A Review of Current Georgia Malaria Control Operations.** *J. National Malaria Soc.* 1948, Sept., v. 7, No. 3, 187–97, 1 fig.

Georgia has experienced all phases of malaria control operations from drug prophylaxis to major drainage but since 1945 has relied on DDT as a residual insecticide. Power sprayers and the normal hand-pumped type of machine have been abandoned in favour of modified knapsack sprayers filled with air from a compressed air tank. In the apparatus now standardized the operator carries on his back two cylinders, one holding compressed air which it discharges through a pressure regulator to the other holding emulsion. The air cylinder is refilled as necessary from an air tank carried on a vehicle. DDT is applied as an emulsion at a dosage which has varied from 100 to 147 mgm. per sq. ft. (3·5 to 5·2 oz. per 1,000 sq. ft.), twice in each season with an interval of 10 to 14 weeks between rounds. The heavier dosage is not found to give comparably increased efficiency justifying the increased costs, and the lower dose is now standardized.

Public co-operation, though on the whole satisfactory, has clearly not been as good as it might be and complaints are fairly numerous. Malaria, diarrhoea and enteric appear to have been reduced, the number of reported cases of malaria in the last three years being 461, 109 and 59. Tentative plans include a ten-dollar reward under certain specified conditions to proven cases of indigenous malaria. *G. Macdonald*

JOBBINS, D. M. Algunos problemas en el control de mosquitos en la carretera interamericana de Centro América. [**Some Mosquito Control Problems along the Inter-American Highway in Central America.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Sept., v. 27, No. 9, 819–23. English version 823–6.

Increasing motor traffic on the completed or nearly completed parts of the Inter-American Highway in Central America has emphasized the importance of the prevention of mosquito-borne diseases at halting places along the route. Many of the larger centres of population in malarious areas have adopted measures of control that afford a reasonable degree of protection. In the smaller towns of the rural lowlands, however, the malaria hazards are considerable. A survey of all such places as are strategically located along the Highway, in all countries between Panama and the United States, was commenced in 1943 by the Pan-American Sanitary Bureau. Malaria risks are largely confined to areas below 1,000 feet : above 3,000 feet malaria and its vectors are found in very restricted areas in Central America. Isolated foci of malaria in the highlands increased in number during the period of highway construction ; this was due to the return of infected labourers to their homes in the hills.

The most important vector is *A. albimanus*; *A. pseudopunctipennis* is probably a secondary vector at high altitudes. Climatic factors in Central America have great influence on mosquito prevalence. Torrential rains of the wet season overload drainage channels built to restrict mosquito breeding, and create fresh breeding places. Temperature and humidity during the dry season greatly restrict mosquito breeding on the Pacific slopes. Some adult Anopheles species survive only long enough in the dry season to lay eggs: the majority of adult females do not survive long enough in the dry season to become infective.

The Pan-American Sanitary Bureau supervised sanitary work in construction camps along the highway, mostly in Costa Rica and Nicaragua, where malaria is an important obstacle to labour efficiency. In temporary camps permanent drainage methods of control could not be justified: in Costa Rica drainage ditching and oil larvicides resulted in excellent control of malaria. Before control was inaugurated in lowland areas in Costa Rica malaria was responsible for from 12 to 40 per cent. of all time lost by American labour employed by contractors.

In Nicaragua where large new camps were constructed on the Rama Road to the Atlantic, which branches eastward from the Highway near Lake Managua and Lake Nicaragua, full reliance for malaria control was placed on DDT, as a larvicide and for the destruction of adult mosquitoes in barracks and other buildings. Control was effective. DDT was used with equal success in some camps in Honduras. Imported malaria cases and carriers were many and required treatment.

In Guatemala between the highland and coastal highway routes which run parallel to the Pacific shore there is a coffee growing area in which *Simulium* or Black Flies breed abundantly in swiftly flowing streams. Sawdust saturated with DDT emulsion concentrate introduced as near the source of the stream as possible was found to be a practical larvicide. Retreatment of streams was necessary at intervals of 1 to 3 weeks. Though effective the practice had to be discontinued. The water in these streams is used as a source of power, for drinking, for washing and processing coffee, and finally for irrigation. The use of the larvicide raised problems of poisoning water supplies; poisoning bees and beneficial insects which come to obtain water from the flumes leading to power plants in the very dry weather; the introduction of toxic materials into the processing of coffee beans; and possible damage to plants by irrigation water.

Norman White

GALVÃO, A. L. A. & DAMASCENO, R. G. Tempo da ação residual do DDT contra o *Anopheles darlingi*. [**Duration of Residual Action of DDT on** *Anopheles darlingi*.] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1948, July, v. 2, No. 1, 17–22, 1 chart.

The English summary appended to the paper is as follows:—

"Studies were made in Belém, Pará, on the duration of the toxic effects of residual DDT on *Anopheles darlingi*. Wooden walls were sprayed with DDT in kerosene solution at 5%, leaving a residue of 2·09 Gm. per square meter. It was found that toxic effects of the insecticide disappeared completely following the eighth month of application.

"Any observations referring to mortality caused by DDT in mosquitoes maintained without feeding should be made from the 8th to the 24th hour after capture; in the 48th hour, the percentage of deaths from natural causes is very high."

PAMPANA, E. J. **Malaria Control by Residual Indoor Spraying with Dichloro-Diphenyl-Trichloroethane (DDT). Survey of Methods for testing Residual Toxicity and of Results.** *Bull. World Health Organization.* 1948, v. 1, No. 2, 253–96, 6 figs. [60 refs.]

This is an analysis of the methods which could be used to estimate residual toxicity of DDT and a review of the literature on each method suggested. The subjects covered are :—

1. Laboratory tests. Experimental exposure chamber ; wall exposure chamber ; recording of data.
2. Controlled field tests. Determination of the residual toxicity of a given surface ; release test ; count of resting mosquitoes ; determination of the survival rate of exposed mosquitoes.
3. Evaluation of reduction in malaria transmission. Anopheline density ; man-biting rate ; sporozoite rate ; malaria incidence.
4. Available evidence of malaria control by DDT spraying.

Details of the methods described are given in full, and include most of the apparatus previously described by SIMMONS and staff [this *Bulletin*, 1946, v. 43, 104, 789]. Each of the methods has its appropriate place ; outlet window traps should be used and estimations of the survival rate of escaping anophelines made more frequently than in the past.

An appendix deals with the cost of malaria control with DDT residual spray. Insecticide itself is a major part of the cost of any scheme. The price of DDT in the U.S.A. is 0·26 U.S. dollars a pound [0·45 Kgm.]. Kerosene as a vehicle is always expensive, its cost sometimes amounting to more than that of DDT. The cost of emulsions varies from 42 per cent. to 74 per cent. of that of kerosene solutions, and suspensions are somewhat cheaper still. There is a useful table which sets out the costs of several campaigns in a manner sufficiently detailed for comparison. They vary from 0·045 to 1·66 U.S. dollars per head per year. There is also a valuable bibliography. *G. Macdonald*

HERING, E. R. & GRIFFIN, J. F. **Two Methods for Application of DDT in the Field.** *U.S. Nav. Med. Bull.* 1948, Sept.–Oct., v. 48, No. 5, 797–802, 4 figs.

This paper reports the use of an apparatus for the production of DDT smoke, and a power sprayer for the distribution of DDT solution as a larvicide, the latter being mounted on an amphibious vehicle, in military manoeuvres.

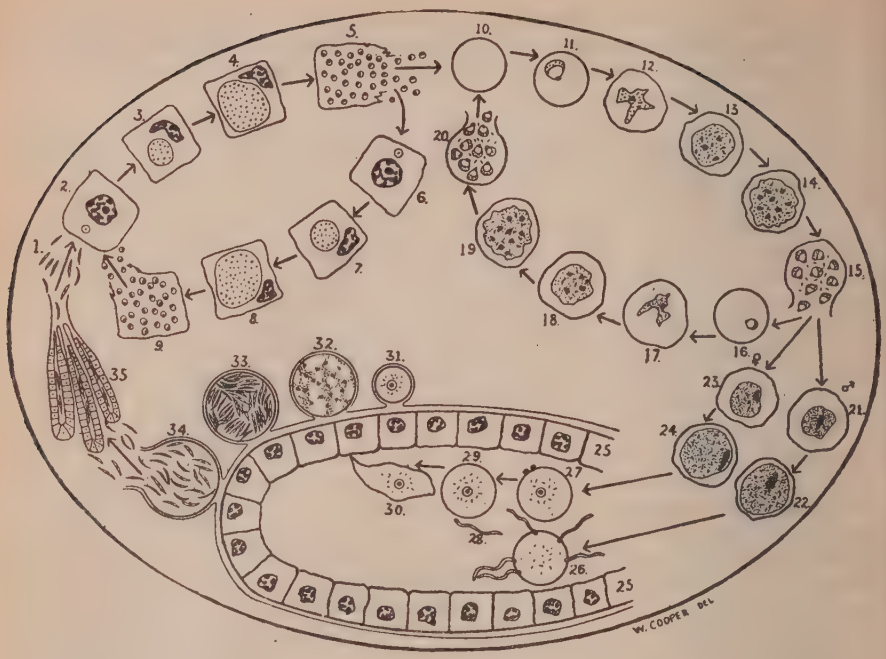
Some specific defects were noted, but the authors were left with little doubt that their use would constitute a material advance in operational military hygiene. *G. Macdonald*

RODHAIN, J. **Susceptibility of the Chimpanzee to *P. malariae* of Human Origin.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 629–31.

This paper is a summary in English of the author's work on *P. malariae* in the chimpanzee [this *Bulletin*, 1948, v. 45, 978].

SHORTT, H. E. **The Life Cycle of *Plasmodium cynomolgi* in its Insect and Mammalian Hosts.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Nov., v. 42, No. 3, 227–30, 35 figs. on pl.

This paper describes the life cycle of the monkey parasite *P. cynomolgi* and includes a summary of the recent work on the exoerythrocytic stages [see this *Bulletin*, 1948, v. 45, 388, 762, 872]. It is accompanied by a useful diagram, reproduced here, which shows the blood, liver and mosquito cycles.



1. Sporozoites from salivary glands of mosquito enter liver cells.

2. Liver cell containing early stage of pre-erythrocytic parasite.

3 and 4. Stages in development of the pre-erythrocytic schizont in liver cells.

5. Fully developed pre-erythrocytic schizont rupturing and releasing pre-erythrocytic merozoites.

6. Liver cell containing merozoite of exo-erythrocytic cycle of schizogony.

7–9. Remaining stages in exo-erythrocytic schizogony ending in second generation of merozoites.

10. Red cell of circulating blood.

11–14. Stages in erythrocytic schizogony in circulating blood.

15. Fully developed erythrocytic schizont rupturing and releasing erythrocytic merozoites and gametocytes.

16–20. Repetition of erythrocytic schizogony.

21 and 22. Development of male gametocyte or microgametocyte in circulating blood.

23 and 24. Development of female gametocyte or macrogametocyte in circulating blood.

25. Wall of stomach of mosquito.

26. Exflagellating microgametocyte producing microgametes in stomach of mosquito.

27. Macrogametocyte extruding polar bodies and so becoming macrogamete.

28. Microgamete free in stomach of mosquito and seeking macrogamete.

29. Zygote, formed by fertilization of macrogamete by a single microgamete.

30. Oökinete or travelling vermicule formed by elongation of zygote. It is about to penetrate epithelial lining of stomach.

31. Oöcyst, formed by oökinete after penetration of stomach wall of mosquito. It lies under elastic membrane on outer surface of stomach.

32 and 33. Stages in development of oöcyst with production of sporozoites.

34. Rupture of mature oöcysts with dispersion of sporozoites most of which enter salivary glands of mosquito.

35. Salivary gland of mosquito containing mature sporozoites.

[Reproduced from the *Transactions of the Royal Society of Tropical Medicine and Hygiene.*]

P. C. C. Garnham

GRAMICCIA, G. Ricerche sulla infezione degli embrioni di pollo con *Plasmodium gallinaceum* (II Nota). [**Infection of Chick Embryos with** *P. gallinaceum.*] *Riv. di Parassit.* Rome. 1948, Sept., v. 9, No. 3, 119–28. English summary (5 lines.)

In a previous paper the author, in collaboration with G. RITA, described attempts to inoculate chick embryos with *P. gallinaceum.* Heavily infected blood was applied to the chorio-allantoic membrane and a small quantity was injected into the vitelline sac. Only two of 15 chickens acquired infection [this *Bulletin*, 1948, v. 45, 158]. Further experiments are now reported. It was found that if the infected blood be drawn from a bird whose internal organs contain exo-erythrocytic forms of the parasite, infection of the embryo was invariably successful. Otherwise only occasional positive results were obtained. The technique adopted is described. *Norman White*

MOULDER, J. W. **Effect of Quinine Treatment of the Host upon the Carbohydrate Metabolism of the Malarial Parasite** *Plasmodium gallinaceum. J. Infect. Dis.* 1948, Nov.–Dec., v. 83, No. 3, 262–70, 2 figs. [27 refs.]

Results by various investigators suggest that quinine exerts its antimalarial effects by a direct action on the parasites. The present investigation deals with the metabolic effects produced in *P. gallinaceum* by treatment of the infected host with the drug. For this study the activities of the parasites from an untreated host were compared with those from the same host 24 hours after treatment with a single dose of quinine intravenously equivalent to 20 mgm. base per kilo. The chickens were inoculated intravenously with infected blood and the final suspension of thrice-washed parasites in Ca-free phosphate saline contained 1 to 2×10^9 parasitized erythrocytes per ml. Oxygen consumption and CO_2 production were measured in a manometric apparatus at 40°C. The small dose of quinine *in vivo* caused a marked change in the metabolism of parasitized cells which, although qualitatively similar, appeared to be greater than that caused by corresponding treatment *in vitro.* The changes noted were recorded in micromoles with respect to 10^{10} square μ of parasite surface area per hour, as used by SILVERMAN *et al.* [this *Bulletin*, 1945, v. 42, 448].

It was found that quinine caused an increase in the rate of disappearance of glucose and of lactate formation, while the oxygen consumption of the parasites was reduced. The increase in O_2 consumption caused by the addition of glucose, lactate or pyruvate to the washed parasitized cells from an untreated chicken was not observed in those from quinine-treated birds. It was concluded that these differences in metabolism resulted from the direct action of quinine on the carbohydrate metabolism of *P. gallinaceum*, after the possible effects of an increase in reticulocytes in the blood and the presence of immune factors had been considered. Quinine did not alter the R.Q. [respiratory quotient] of parasitized erythrocytes metabolizing glucose, but when lactate and pyruvate were used as substrates after quinine treatment O_2 uptake and the utilization of these substrates was decreased, while the R.Q. and O_2/substrate ratios were unaltered. The results of quinine treatment on the oxidation of the three substrates mentioned suggest that in the anaerobic phase their breakdown is not affected by the drug, while in the aerobic phase the complete oxidation of pyruvate via the tricarboxylic acid cycle is inhibited [*cf.* SILVERMAN *et al.*, above]. Since KELSEY *et al.* [this *Bulletin*, 1944, v. 41, 11] have shown that quinine disappeared from the blood in a few hours, the present results indicate that the inhibition of carbohydrate metabolism by quinine is irreversible or that an effective metabolite of this substance continues to act.

J. D. Fulton

TRAGER, W. **The Resistance of Egg-laying Ducks to Infection by the Malaria Parasite** *Plasmodium lophurae*. *J. Parasitology*. 1948, Oct., v. 34, No. 5, 389–93, 1 fig. [10 refs.]

It was noticed that a certain number of adult ducks infected with *P. lophurae* failed to respond in the usual manner to the disease : the parasites were low in number and abnormal in morphology. The meaning of this was elucidated by repeating the experiments on 3 groups of ducks 6–7 months old. One group was composed of males, the second group of females with inactive ovaries, and the third group of females with active ovaries. They all received equivalent and very heavy doses of *P. lophurae*. Most of the ducks in the first two groups developed heavy infections, while the egg-laying group showed a poor response, the parasites not multiplying in nine out of 12 ducks in this last group.

The author then proceeded to correlate this finding with the amount of biotin or biotin-active lipoids in the plasma of the infected birds. A high biotin content was found to be associated with egg-laying activity and with a relative resistance to the malarial infection ; male ducks had the lowest biotin concentrations and conversely were very susceptible to the disease.

P. C. C. Garnham

THOMPSON, P. E., with the technical assistance of Anita BAYLES, D. L. BUSH & Betty L. LILLIGREN. **On the Ability of** *Plasmodium lophurae* **to acquire Resistance to Chlorguanide, Camoquin and Chloroquine.** *J. Infect. Dis.* 1948, Nov.–Dec., v. 83, No. 3, 250–55. [15 refs.]

The development of acquired resistance to paludrine (chlorguanide) by *P. gallinaceum* was recently described [this *Bulletin*, 1947, v. 44, 969, 970 ; 1948, v. 45, 158]. A similar resistance has now been shown to occur in the case of *P. lophurae* but could not be obtained with Camoquin (SN 10,751) or with chloroquine, both 4-aminoquinoline derivatives. White Leghorn chicks 4 to 8 days old were inoculated intravenously with parasitized blood and the drug was administered in the diet for some hours previous to infection. They were maintained on a light and dark schedule for alternate periods of 4 hours, in order that the intake of drug should be as constant as possible. The level of drug was such as to cause a 50 per cent. suppression of the infection. Under these conditions the parasites were kept in almost continuous contact with it. Subinoculations were made twice weekly over a period of 211 days and included 60 passages. When testing for acquired resistance, suppression of infection to the extent of 50 per cent. at or near the peak of parasitaemia was accepted as indicating that a drug was still effective. Within 28 days in which 8 passages were made, resistance became evident in the paludrine-treated birds and was correlated with the morphological appearance of the parasites. The resistance developed only gradually in contrast to that obtained with *P. gallinaceum*. The resistance to paludrine did not affect the result of treatment with plasmoquine [pamaquin], quinine, atebrin [mepacrine], chloroquine or Camoquin. Experiments on the persistence of resistance after mosquito transmission were not made.

J. D. Fulton

BARANGER, P. & FILER, M. K. Contribution à l'étude des mélanges d'alcaloïdes du quinquina. [**A Study of Mixtures of Cinchona Alkaloids.**] *Ann. Inst. Pasteur*. 1948, Oct., v. 75, No. 4, 329–37.

In a previous paper [this *Bulletin* 1944, v. 41, 103] the senior author, with THOMAS, reported, from tests carried out on canaries infected with *P. relictum*, that total alkaloids from different cinchona barks gave better therapeutic results than quinine alone. The results were poor, however, when the quinine

was removed. They have now found that certain combinations of the four main alkaloids in pairs give more favourable results in blood-induced infections of *P. relictum* and *P. gallinaceum* than quinine alone. It is possible that a synergistic effect results from the action of the alkaloids in combination on different stages in the life cycle of the parasites. Cinchonine seems to have a special mode of action, since its effects are produced at very much lower plasma concentrations than in the case of the three other alkaloids. In the case of *P. relictum*, the activity of each alkaloid was similar. There appeared to be a synergistic action between cinchonidine and quinine. Under the experimental conditions the results confirmed the previous findings that the activity of the total alkaloids from different barks is equal or superior to quinine or the other pure alkaloids. The percentage of quinine in the total extract did not appear to determine the activity of the mixtures. Similar experiments with mosquito-transmitted infections appear desirable. *J. D. Fulton*

ASENJO, C. F., FREIRE DE GUZMÁN, A. R., MAYORAL DE ASENJO, A. G. & DE LOPEZ CANDAL, J. G. **A Chemical Study of the Molinillo Plant** (*Leonitis nepetaefolia*, **L.), with special reference to its Seed.** *Puerto Rico J. Pub. Health & Trop. Med.* 1948, Sept., v. 24, No. 1, 44–56, 2 figs. [Refs. in footnotes.] [Spanish version 57–68.]

" Chick and canary tests gave negative results for antimalarial activity with the exception of the seed that showed a slight activity."

PARAENSE, W. L. Observações preliminares sobre o ciclo exoeritrocitário do *Plasmodium juxtanucleare* Versiani e Gomes, 1941. [**Preliminary Observations on the Exoerythrocytic Schizogony of** *Plasmodium juxtanucleare* **Versiani and Gomes, 1941.**] *Mem. Inst. Oswaldo Cruz.* 1947, Dec., v. 45, No. 4, 813–23, 1 graph & 15 coloured figs. on pl. English summary.

BARRETO [this *Bulletin* 1944, v. 41, 732] described briefly exoerythrocytic schizonts of this malarial parasite of the domestic fowl. He observed the forms solely in the cerebral capillaries 34 to 52 days after inoculation, and the schizonts he figured were small bodies with a maximum of 19 blocks of chromatin. Other observers in South and Central America have hitherto failed to confirm this work, but now Paraense has been successful in obtaining exoerythrocytic forms of a different type from those described by Barreto. He recovered the strain from a fowl bought in the Minas Gerais State of Brazil and maintained it in Light Sussex, Rhode Island and Leghorn chicks. The infection was passaged intravenously and the birds were sacrificed at different intervals after inoculation. Smears were made of the spleen, bone-marrow, liver, lungs and brain, and exoerythrocytic schizonts were found in these organs in numbers following the above order, being most numerous in the spleen (up to 5 parasites per field under the 1/12th in. objective) and fewest in the brain. The schizonts were first seen 9 days after inoculation and were most plentiful during the third week. If quinine (150 mgm. per kilo daily) is administered after the fifth day of the patent period, parasitaemia is depressed to 4 per cent. or less, but the chicks die from the exoerythrocytic infection.

[The author does not describe in the text the morphology of these parasites, but illustrates them by a coloured plate. In this plate may be seen rather small schizonts occupying macrophage or endothelial cells and containing apparently as many as 80 merozoites. Mosquito transmission of *P. juxtanucleare* has still to be effected, so the cryptozoites of the pre-erythrocytic cycle remain undescribed.] *P. C. C. Garnham*

SERGENT, Ed. & SERGENT, Et. *Haemoproteus wenyoni* nov. sp., parasite du moineau algérien retrouvé chez des canaris élevés en cage. [*Haemoproteus wenyoni* **sp. nov. Parasite of the Algerian Sparrow, recovered in Cage-Reared Canaries.**] *Arch. Inst. Pasteur d'Algérie.* 1948, Dec., v. 26, No. 4, 394–6, 2 figs.

A *Haemoproteus* was first found in sparrows by GRASSI and FELETTI in 1890, in Sicily; it was redescribed by the present authors in 1907 from Algeria, while WENYON in 1911 discovered the asexual forms in the sparrows of Bagdad. The species has remained nameless until now when it receives the name of *H. wenyoni*. It differs from most other forms by a marked irregularity of outline. The younger gametocytes are small oval bodies.

Large numbers of canaries are kept in cages in Algiers; in the neighbouring trees are thousands of sparrows. It is not surprising, therefore, that the arthropod-borne parasites of the latter eventually infect the caged birds. The sparrows are heavily infected with *Haemoproteus*, as are 5 per cent. of the canaries: 100 per cent. of sparrows and 4 per cent. of the canaries show *Plasmodium relictum*, 13 per cent. of the sparrows and 0·04 per cent. of the canaries show *Eufilaria sergenti*. The indigenous sparrow thus constitutes a reservoir of the local parasites and this situation is parallelled in human beings, the non-immune immigrant becoming infected with malaria and other endemic diseases.

[This paper is doubly *in memoriam*: since it was written, two of the chief characters have died, Dr. Etienne SERGENT in August, 1948 and Dr. C. M. WENYON in October.] *P. C. C. Garnham*

BLACKWATER FEVER

POURSINES, Y. & MOUSTARDIER, G. Considérations pathogéniques sur le mécanisme de l'anurie dans la fièvre bilieuse hémoglobinurique. A propos des lesions histologiques du rein. Applications thérapeutiques. [**Pathological Processes involved in producing Anuria in Blackwater Fever: Histology of Kidney Lesions: Therapeutic Applications.**] *Méd. Trop.* Marseilles. 1948, July–Aug.–Sept.–Oct., v. 8, No. 4, 451–7, 4 figs. [11 refs.]

This account of the pathological processes involved in the production of anuria in blackwater fever does not differ substantially from that given elsewhere by the same authors [see this *Bulletin*, 1949, v. 46, 120]. Reference to treatment of anuria by intravenous novocaine is of a general nature and not directly concerned with blackwater fever. *B. G. Maegraith*

TRYPANOSOMIASIS

GUYAUX, R. Note sur l'épidémiologie des trypanosomiases bovines en milieu d'élevage indigène au Kivu. [**A Note on the Epidemiology of Bovine Trypanosomiasis in an African Stock-Breeding Centre in Kivu.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Sept. 31, v. 28, No. 3, 345–54, 4 graphs.

HARVEY, S. C. **Anomalous Effects of Zinc-Insulin upon** *Trypanosoma hippicum*. *Proc. Soc. Exper. Biol. & Med.* 1948, Dec., v. 69, No. 3, 555–7, 2 figs.

LILJESTRAND, A. **Assay of the Curative Action of Neoarsphenamine by Time-Mortality Data.** *J. Pharm. & Pharmacol.* 1949, Feb., v. 1, No. 2, 78–86, 2 figs. [12 refs.]

NEGHME, A. & ROMÁN, J. **Present State of Chagas' Disease Surveys in Chile.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 835–9.

This is a report of a survey carried out between August 1944 and December 1947 in the Provinces of Tarapacá, Atacama, Coquimbo, Aconcagua, Valparaiso and Santiago: 12,581 persons were examined by xenodiagnosis and in many cases blood was taken for serological tests. From examination of random samples in the endemic zones an average of 12 per cent. was found infected with *T. cruzi*. During the period of investigation 1,631 human infections have been found. The distribution by Provinces is given in a Table; the chief were Santiago (734) and Coquimbo (441). Machado-Guerreiro reactions were performed in 8,142 individuals from endemic zones and 17 per cent. proved positive and another 10·9 per cent. were suspicious (2-plus). [Some authors dispute the specificity of this test, so the authors themselves tried it on 2,000 sera from University students with no suspicion of any epidemiological antecedents of Chagas's disease; only two were positive.] Of 3,182 domestic animals, dogs and cats, tested by xenodiagnosis, 426 or 13·4 per cent., were positive; no rabbit or guineapig was positive out of 126 examined and only 11 out of 698 "wild animals", and 8 of these were the indigenous Chilian rodent, *Octodon degus* Molina.

They have also examined 20,614 triatomids from different endemic zones; the percentage of infection varied, naturally, from zone to zone, but, of the whole, 9,164 (44 per cent.) were infected—sufficient to explain the widespread infection throughout the country. For prophylaxis, the main object is, of course, to build vinchuca-proof houses, but in the meantime insecticides play a major part and DDT has been largely used, 5 per cent. in kerosene, or of this strength prepared from a basic solution in xylol added to Triton-X-100 as a detergent: 830 houses have been sprayed, with 1,047 gm. per house. Flies, fleas and bed-bugs have practically disappeared. The results as regards Triatomids were not so good, unless the infestation was very slight, but they were reduced below the initial levels. With Gammexane the results were practically the same as those with DDT. Chlordane (or Oktachlor), $C_{10}H_6Cl_8$, even in a 5 per cent. concentration, had little noticeable action on triatomids. *H. Harold Scott*

LEISHMANIASIS

ADLER, S. & ZUCKERMAN, A. **Observations on a Strain of *Leishmania tropica* after Prolonged Cultivation: Notes on Infectivity and Immunity.** *Ann. Trop. Med. & Parasit.* 1948, Sept., v. 42, No. 2, 178–83.

A record is given of the properties of a strain (Ber) of *Leishmania tropica* originally isolated from a sandfly, *Phlebotomus papatasii* and subsequently maintained in culture for 22 years.

The strain at first behaved in *P. papatasii* in the manner typical of local strains of *L. tropica* and gave the same serological reactions. It was also infective to a human volunteer and produced typical dermal lesions. Twenty to twenty-two years later, eighteen hamsters inoculated intraperitoneally, intrasplenically, or by both methods, remained uninfected although control animals inoculated with cultures of recently isolated local strains all developed visceral infections.

Ten hamsters, refractory to the Ber strain, when inoculated with a strain known to be infective to hamsters, gave nine infections indicating that the non-infecting Ber strain gave no appreciable immunity against a known infective strain.

The results of inoculating the Ber strain in man were surprising. As recently isolated strains of *L. tropica* are fatal to Syrian hamsters but produce only harmless local lesions in man, it seemed likely that the Ber strain, which was non-infective to hamsters would be similarly harmless to man. It was found, on the contrary, that when it was inoculated intradermally in two human volunteers, both developed lesions containing numerous L.D. bodies. Both cases also gave a positive leishmanin reaction. Cultures from these cases were non-infective to hamsters.

In one case, originally infected in 1925 with flagellates obtained from a wild-caught sandfly, a lesion developed which was cured spontaneously in about two years. This case proved immune to frequent subsequent attempts at re-infection and the skin test remained constantly positive between 1927 and 1938. In 1946, a phenolized suspension of the Ber strain was inoculated intradermally and produced an erythematous area of 4 in. in diameter at 48 hours which began to recede after 72 hours.

Five days after this inoculation, living flagellates of a strain known to be infective to man and hamster were inoculated. This inoculation produced an erythema of 4 in. diameter with a central necrotic area. There was a temperature reaction. After 24 hours, a culture from the necrotic area yielded positive results for leishmania and was bacteriologically sterile. Later cultures remained sterile both as regards leishmania and bacteria. The affected area developed lymphangitis and blisters, the former persisting for a week. The necrotic area became haemorrhagic and eventually healed leaving a scar. The sequence of events would appear to justify the conclusion that it was an example of an Arthus reaction produced by a protozoon.

The Ber strain showed a reduced infectivity for *Phlebotomus papatasii* as compared with recently isolated strains. *H. E. Shortt*

AUERBACH, S. H. & BUCHHOLZ, R. R. **Cutaneous Leishmaniasis in the United States. Report of a Case in a Veteran.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 831–4, 3 figs.

"The thirty-first case of cutaneous leishmaniasis reported from the United States and Canada is presented. All were exogenous. This patient was a returned veteran who had been exposed to infection in the Mediterranean area. The disease responded satisfactorily to radiation therapy."

RITTERSON, A. L. & STAUBER, L. A. **Protein Intake and Leishmaniasis in the Hamster.** *Proc. Soc. Exper. Biol. & Med.* 1949, Jan., v. 70, No. 1, 47–50, 2 figs.

"Protein intake influences the course of leishmaniasis in the hamster, deficient diets leading to earlier emaciation and death. Excess dietary protein seems to favor survival."

FEVERS OF THE TYPHUS GROUP

D'IGNAZIO, C. & CODELEONCINI, E. L'opera dei Medici Italiani nella lotta contro il dermotifo in Etiopia (1937–1947). [**The Work of Italian Medical Men in the Campaign against Typhus Fever in Ethiopia.**] *Acta Med. Italica.* 1948, Nov., v. 3, No. 11, 295–303. [42 refs.]

In an editorial preface this long article is referred to as a documented account of ten years of intense research and organized effort by Italian medical men.

This effort is described as all the more noble, and even heroic, because it was carried out in conditions of disturbance associated with a lost war and of discouragement due to uncertain future prospects.

In such circumstances it is certainly surprising to find that about 90 articles on the typhus fevers of Ethiopia have been published or prepared for publication during the period. Nearly all of these have been written by the authors and Dr. G. MARIANI.

Many references to the work will be found in this *Bulletin*.

Louse-borne typhus was by far the most common form of the disease, but the occurrence of "benign flea typhus" has been definitely established, and it is said that both tick typhus and mite typhus have been clearly identified on clinical grounds, supported by serological and laboratory studies, which though not yet complete, are regarded as justifying the authors in concluding that the diseases occur in Ethiopia. *John W. D. Megaw*

MONTESTRUC, E. Contribution à l'étude des rickettsioses à la Martinique. (Comportement des sérums des sujets normaux, des fébricitants et des femmes enceintes vis-à-vis des *Protéus OX19, OX2, OXK, OXL* et des rickettsies des typhus épidémique et murin). [**A Study of the Rickettsial Diseases of Martinique (Weil-Felix and Rickettsia-Agglutination Reactions among Normal Persons, Febrile Patients, and Pregnant Women.**] *Arch. Inst. Pasteur de la Martinique*. 1949, Jan., v. 2, No. 1, 3–20.

CIACCIO, G. Essais d'inoculation de *Rickettsia prowazeki* et *Rickettsia mooseri* chez les insectes. Étude des anticorps spécifiques. [**Experiments in Inoculation of Insects with *Rickettsia prowazeki* and *R. mooseri*. Study of Antibodies.**] *Ann. Inst. Pasteur*. 1948, Dec., v. 75, No. 6, 585–6.

The following is a translation of the author's summary :—

Pathogenic rickettsiae (*R. prowazeki* and *R. mooseri*) can be adapted to insects other than those which are ordinarily their hosts. The chrysalis of *Bombyx mori* and the larva of *Tenebrio molitor* support the survival of the virus, but nevertheless do not develop anti-rickettsial agglutinins [see also this *Bulletin*, 1947, v. 44, 703]. *H. J. O'D. Burke-Gaffney*

GALLARDO, F. P. & FOX, J. P. **Infection of Guinea Pigs with Massive Doses of Rickettsiae of Epidemic and Murine Typhus.** *J. Immunology*. 1948, Dec., v. 60, No. 4, 455–63. [12 refs.]

The authors have studied the effects produced by the inoculation of massive doses of epidemic and murine rickettsiae into guineapigs by the intraabdominal and intracardiac routes. Highly concentrated suspensions of infected yolk sacs and cotton-rat livers were employed ; these caused severe, often fatal, disease, especially when administered by the intracardiac route.

The disease was more severe in large guineapigs than in small, and younger, ones ; the authors suggest that this difference in susceptibility may be related to the greater severity of typhus fever in elderly patients.

Although the incubation period after massive doses was only two or three days the illness was a true infection, not an intoxication of the kind observed in mice inoculated with large doses of rickettsiae.

The authors believe that the employment of large doses is likely to be useful in the study of the chemotherapy of typhus fever and in the development of improved methods of carrying out serum-neutralization tests.

Among the four strains of epidemic rickettsiae employed was the "E" strain originally isolated in Madrid by CLAVERO and PÉREZ GALLARDO in 1943 [this *Bulletin*, 1944, v. 41, 24] ; this was found to have maintained its low virulence

through 259 passages in embryo chicks, it also produced a lower degree of immunity in guineapigs than the virulent strains commonly used. [See this *Bulletin*, 1949, v. 46, 24].

The infections caused in guineapigs by massive doses were less severe in the hot season (June) than in the cold season (January and March).

John W. D. Megaw

LIU, Wei-t'ung, CHANG, Huei-ching & WANG, P'ei-jen. **Further Observations on Complement Fixation in Typhus Fever.** *J. Infect. Dis.* 1948, Nov.–Dec., v. 83, No. 3, 207–19. [22 refs.]

[See also this *Bulletin*, 1949, v. 46, 24.]

D'IGNAZIO, C. & MUSI, P. S. Rara complicanza oculare in un caso di dermotifo. [**A Rare Ocular Complication of Typhus.**] *Acta Med. Italica.* 1948, Dec., v. 3, No. 12, 315–18. English summary (3 lines).

The English summary appended to the paper is as follows :—

" The authors describe a case of optical neuritis in a patient suffering with typhus and point out some considerations about this rare complication."

MOOSER, H. **On the Nomenclature of the Agent of Murine Typhus.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 841–3. [18 refs.]

The author raises strong objections to the proposal by PHILIP that the name *Rickettsia mooseri* should be changed to *R. typhi* or *R. prowazeki* var. *typhi* [see this *Bulletin*, 1943, v. 40, 828].

The reason given for making this proposal is that WOLBACH and TODD in 1920 gave the name *Dermacentroxenus typhi* to the organism found in a form of Mexican typhus which Wolbach, in a personal communication to Philip, said he believed to have been probably of the murine type.

Mooser insists that it would have been utterly impossible for Wolbach to have made a reliable diagnosis of murine typhus on the strength of the available evidence, which consisted in the histological characters of sections of skin of a few patients. Mooser mentions a case in which experts of the highest standing in 1931 made a confident diagnosis of epidemic typhus on the strength of a complete histological examination, but later had to admit that the disease was probably Rocky Mountain spotted fever. Reasons are given for believing that the cases seen by Wolbach were far more likely to have been of the epidemic rather than of the murine type, so that the name given by Philip " has no standing." [See the comment on the abstract above.]

John W. D. Megaw

DIAZ-RIVERA, R. S., GUZMAN ACOSTA, C., COLLAZO, P. J. & POMALES LEBRON, A. **Effect of Para-Aminobenzoic Acid on Murine Typhus. A Clinical Study of 60 Cases.** *Amer. J. Med. Sci.* 1949, Jan., v. 217, No. 1, 13–20, 1 fig. [18 refs.]

" During the past two years " 33 patients suffering from murine typhus were treated by large doses of PABA, and 27 patients " picked at random " were kept as untreated controls.

Treatment was started, on the average, 6·5 days after the onset. The only effect on the rash was that it disappeared more rapidly in the treated. Two of the treated had severe nausea and vomiting, but so also had some of the untreated controls.

Improvement in the general condition was usually evident within one or two days; the average duration of the fever was 8·7 days in the treated, and 15 days in the control, patients. There was no death in either group.

In 14 cases the treatment was started after the 7th day, yet in 6 of these the results were favourable.

The dosage was 4·0 gm. initially, then 2·0 gm. every two hours till convalescence was established. The total amount given was as much as 219 gm. in some cases. *John W. D. Megaw*

FitzPatrick, Florence K. **Effect of an Analogue of DDT on Experimental Murine Typhus.** *Proc. Soc. Exper. Biol. & Med.* 1949, Jan., v. 70, No. 1, 90–91.

"The nitro analogue of DDT when given in the diet for 7 days to mice infected with murine typhus resulted in a degree of survival on the 7th day equal to that obtained when 4 times the amount of PABA was administered. After the 7th day, when the drug was withdrawn, more PABA-treated mice succumbed, indicating that the nitro analogue is a better rickettsiacidal agent. The oral toxicity of the compound for mice appears to be of a low order."

Ruiz Sanchez, F. & Ruiz Sanchez, A. El tratamiento del tifo exantematico con aureomicina. Reporte preliminar. **Treatment of Typhus Fever by Aureomycin.** *Medicina.* Mexico. 1948, Dec. 25, v. 28, No. 570, 521–7, 5 graphs.

Five cases of typhus fever, probably of the murine type, were treated by oral administration of aureomycin. The daily dose was 300 mgm. per kgm. of body weight given in divided doses every three hours. In the earlier cases the treatment was continued for several days, but later it was found that treatment for one or two days was equally effective. In every case the response to treatment was prompt and satisfactory.

The only signs of intoxication were occasional nausea, vomiting, and diarrhoea, but these soon disappeared and did not necessitate interruption of the treatment. *John W. D. Megaw*

Smadel, J. E. **Chloromycetin in the Treatment of Typhus Fevers.** *Bull. U.S. Army Med. Dept.* 1949, Feb., v. 9, No. 2, 117–23, 3 figs.

This paper consists chiefly of a succinct summary of recent work on the treatment of fevers of the typhus group by chloromycetin. This work, most of which was done by the author, has been dealt with in recent numbers of this *Bulletin*.

Reference is made to a trial of the drug as a prophylactic: a group of 40 volunteers exposed to special risk of infection by scrub typhus in a hyperendemic area near Kuala Lumpur remained free from clinical symptoms during the period of exposure and for a week after ceasing to take the drug, but "thereafter, a considerable proportion" of them were attacked so that the drug seemed to have acted as a temporary suppressive.

Among 24 control persons exposed to the same risk there were 17 cases of the disease with onset between the 12th and 22nd day after initial exposure.

Further studies on the chemoprophylaxis of the disease are being initiated.

John W. D. Megaw

STOKER, M. G. P. **Serological Evidence of Q Fever in Great Britain.** *Lancet.* 1949, Jan. 29, 178–9. [14 refs.]

Among 24 sera from sporadic cases of atypical pneumonia, three were found to give positive complement-fixation reactions against an American and an Italian strain of Q fever antigen supplied by Dr. Herald Cox.

Two of the reacting patients had been living at a Royal Air Force Station near Salisbury, Wiltshire for some time before the onset, which was in April, 1948, in one case, and February, 1948, in the other. There had been only one other case of atypical pneumonia at this station during the first half of 1948, but no sample of serum could be obtained.

The third patient was admitted to the Kingston County Hospital, near London, in June, 1948; this patient and one of the other two had never been abroad so that the infection must have occurred in England. The titres of the reactions were 1–40 to 1–80, and the results of the test were confirmed by Dr. Ross Gauld at the Army Medical School, Washington, in both of the sera submitted to him. *John W. D. Megaw*

VISCHER, W. A. Gehäuftes Auftreten von Q-Fieber in einer Rekrutenschule. [**An Epidemic of Q Fever in a School for Recruits.**] *Schweiz. med. Woch.* 1949, Feb. 19, v. 79, No. 7, 137–8.

During the months of March and April, 1948, an explosive outbreak of Q fever occurred in a school for recruits at Monte Ceneri in Switzerland. There were 56 cases among 450 young recruits.

The source of infection could not be discovered; it was suspected that inhalation of infected dust was responsible because the outbreak occurred in fine and dry weather. Some cases were found to have occurred among the inhabitants of a neighbouring town which was visited by the recruits when off duty. *John W. D. Megaw*

BECK, M. D., BELL, J. A., SHAW, E. W. & HUEBNER, R. J. **Q Fever Studies in Southern California. II. An Epidemiological Study of 300 Cases.** *Pub. Health Rep.* Wash. 1949, Jan. 14, v. 64, No. 2, 41–56, 1 map. [26 refs.]

This study formed part of a combined investigation by the National and California Health Services into the epidemiology of Q fever.

A detailed survey was made of the epidemiological conditions associated with 300 proved cases of the disease in the Los Angeles area.

The disease occurred throughout the area at all seasons, and year after year. Most of the patients were adult males. Transmission of infection appeared to be associated with one of the following circumstances:—(1) Employment in the dairy or live-stock industry; (2) residence near a dairy or live-stock yard; (3) the use of raw milk by the household.

None of these three factors could by itself have been responsible for the infection in more than half of the cases, but in 78 per cent. there was clear evidence that one or more of the factors could have been concerned, and this percentage was greatly in excess of that applying to the rest of the population of the affected area. Further studies are in progress to discover the relative importance of each factor.

A useful bibliography supplies references to 26 papers on Q fever.

John W. D. Megaw

JELLISON, W. L., HUEBNER, R. J., BECK, M. D., PARKER, R. R. & BELL, E. J. **Q Fever Studies in Southern California. VIII. Recovery of *Coxiella burneti* from Butter made from Naturally Infected and Unpasteurized Milk.** *Pub. Health Rep.* Wash. 1948, Dec. 31, v. 63, No. 53, 1712–13.

High-titre complement-fixation reactions against *Coxiella* [*Rickettsia*] *burneti* were found to occur in guineapigs inoculated with refrigerated butter made from the raw milk of cows infected with Q fever. The butter was still infective after being kept in the refrigerator (below 0°C.) for 41 days. A strain of the rickettsia from the butter was isolated and established in a guineapig.

John W. D. Megaw

JANTON, O. H., BONDI, A., Jr. & SIGEL, M. M. **Q Fever : Report of a Case in Pennsylvania.** *Ann. Intern. Med.* 1949, Jan., v. 30, No. 1, 180–84, 1 fig. [20 refs.]

" The first report of a serologically authenticated case of naturally acquired Q fever in eastern United States is presented. The clinical features are discussed in detail with emphasis placed on the consideration of this disease in the differential diagnosis of respiratory disorders. The possible mode of transmission is discussed."

DE RODANICHE, E. C. & RODANICHE, A. **Studies on Q Fever in Panama.** *Amer. J. Hyg.* 1949, Jan., v. 49, No. 1, 67–75. [24 refs.]

Sera of 26 patients, including 17 diagnosed as suffering from atypical pneumonia, were tested by the complement-fixation reaction for Q fever. Only three gave a significant reaction, and from one of these a strain of *Rickettsia burneti* was isolated.

In the Gorgas Memorial Hospital nine workers were engaged in the study of Q fever rickettsiae from March, 1947, but no case of obvious infection occurred till February, 1948, when one of them had a severe attack and a strain of *R. burneti* was isolated from his blood. This worker was also engaged on field work in the course of which he was often bitten by ticks, so that infection may not have been acquired in the laboratory.

Four of the other workers were found to have positive fixation reactions at titres of 1–128 ; 1–64 ; 1–16, and 1–8, respectively, but none of them had suffered from any illness suggestive of Q fever. The worker with a titre of 1–128 was known to have had a negative reaction about four months previously so it appeared that he must have had a sub-clinical infection.

John W. D. Megaw

PHILIP, C. B. **Observations on Experimental Q Fever.** *J. Parasitology.* 1948, Dec., v. 34, No. 6, 457–64.

Most of the experimental work described in this paper was carried out before the recent war. Some of the chief findings are as follows.

Q fever infection could not be transmitted, even mechanically, by the bite of *Aëdes aegypti* from infected to susceptible guineapigs. The mosquitoes were allowed to feed on the test guineapigs immediately after making the infected blood meal and also 10 to 30 days afterwards.

Infection rapidly disappeared from the bodies of the mosquitoes, as was shown by the failure to infect guineapigs with suspensions of the guts of the insects after an infecting feed.

Suspensions of infected *Dermacentor andersoni* were infective to guineapigs in dilutions as high as 1–500,000 millions, and in very high dilutions even after

passage through Berkefeld N and W candles. Dried faeces of infected *D. andersoni* were still infective after storage for 586 days, and after storage at room temperature, with 70 per cent. humidity, for nearly six years they still showed recognizable organisms and produced immunity in inoculated guineapigs, though strains could not be isolated from the animals or by yolk-sac culture.

Infected faeces of ticks and suspensions of spleens of infected guineapigs caused infection in guineapigs by application to the unbroken skin. Powdered tick faeces dusted into the nostrils, eyes, or mouth, of guineapigs caused infection. *D. andersoni*, infected during the nymph stage and kept for 65 and 127 days, at 35°F., were still highly infective. This result is in contrast with what happens in ticks infected with *R. rickettsi*, which need a "reactivating" blood meal before becoming infective in similar circumstances.

Infection was recovered from house-flies caught in a room in which infected guineapigs were kept, but house-flies did not appear to be capable of transmitting infection because when given free access at the same time to infected guineapigs in one set of cages and susceptible guineapigs in other cages no transmission occurred.

Flies fed on infected tick faeces and on infected spleen pulp of guineapigs became contaminated with the rickettsiae ; this was shown by the production of the disease in guineapigs inoculated with suspensions of the bodies of the flies.

John W. D. Megaw

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WOLFE, D. M. & KORNFELD, Lottie. With technical assistance of Lois GALLIK. **Conglutinating Complement Absorption Test compared with Hemolytic Complement-Fixation Reactions using Q Fever Immune Bovine Serum.** *Proc. Soc. Exper. Biol. & Med.* 1948, Nov., v. 69, No. 2, 251–5.

The essential difference between the Conglutination Complement-Absorption Test and the ordinary complement-absorption test is that in the former clumping instead of haemolysis of red cells serves as an indicator of the presence of unabsorbed complement.

The occurrence of conglutination was first described by BORDET and STRENG in 1909, and a test for glanders based on this phenomenon has been worked out by HOLE and COOMBS in 1947. The latter workers observed that clumping of sheep red cells occurs when a suspension of them is mixed with heat-inactivated bovine serum and fresh unheated serum of a horse, dog, or cat. The bovine serum contains a natural antibody which sensitizes the sheep cells, and also a conglutinin ; the fresh serum contains complement.

Technical details of the application of the test to the detection of Q fever in cattle are given in the paper.

From the tests already carried out, the authors conclude that the reaction is likely to prove more sensitive and more specific than the complement-absorption test in common use. Further studies are said to be in progress.

John W. D. Megaw

SHEPARD, C. C. **Q Fever : a Serological Survey of Bovine Serums in the United States.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 849–55. [11 refs.]

Through the organization which exists for testing cattle for brucellosis it was possible to obtain samples of serum from 1,789 cattle from 37 States of the U.S.A. other than California.

Complement-fixation tests showed that 27 of the cattle were, or had been, infected with Q fever. Positive samples originated from the following States :— Pennsylvania, Wisconsin, Minnesota, Missouri, North Dakota, Nebraska, Kansas, Virginia, Kentucky, Mississippi, Texas, Colorado, New Mexico, Arizona,

Washington, and Oregon. In Pennsylvania there was only one positive among 99 samples; in Nebraska, Missouri and Wisconsin there were three positives among 48 to 50 samples; in all the other States mentioned there were either one or two positives in 47 to 50 samples.

Only two of the positive samples came from the eastern one-third of the U.S.A.

A rickettsia-agglutination test was carried out on a large number of random samples of the sera with the surprising result that there were 68 per cent. of positive reactions at titres of 1-5 to 1-125. These reactions were regarded as non-specific and as being due to the presence of "natural" antibodies.

In a footnote the author states that since this paper was submitted for publication the official name of Q fever rickettsia has been changed from *R. burneti* to *Coxiella burneti*.

[No mention is made of the official agency by which this change was decreed. The change was proposed by PHILIP in 1943 (see this *Bulletin*, 1943, v. 40, 828). In the same article Philip proposed that the name *R. mooseri* should be changed to *R. typhi*; this proposal has been severely criticized by MOOSER (see below). Philip also advocated the use of the name *Dermacentroxenus rickettsi* instead of the more usual *R. rickettsi*.

It is to be hoped that definite evidence of the necessity for these changes will be provided, otherwise there may be passive resistance to their acceptance.]

John W. D. Megaw

OLIPHANT, J. W., GORDON, D. A., MEIS, A. & PARKER, R. R. **Q Fever in Laundry Workers, presumably transmitted from Contaminated Clothing.** *Amer. J. Hyg.* 1949, Jan., v. 49, No. 1, 76–82, 3 figs. [18 refs.]

Recently three cases of Q fever and three cases of subclinical infection occurred among 13 persons employed in a laundry in which soiled overalls, towels, etc. from the Rocky Mountain Laboratory, Montana, were laundered.

The six persons infected were the only ones engaged in handling the articles before laundering. No likely source of infection other than the soiled articles was discovered.

John W. D. Megaw

SPICKNALL, C. G., TERRY, L. L. & HUEBNER, R. J. **Treatment of Q Fever with Streptomycin. A Case Report.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 845–7, 1 fig. [13 refs.]

There was "apparent response to streptomycin".

YELLOW FEVER

HADDOW, A. J., SMITHBURN, K. C., DICK, G. W. A., KITCHEN, S. F. & LUMSDEN, W. H. R. **Implication of the Mosquito *Aëdes* (*Stegomyia*) *africanus* Theobald in the Forest Cycle of Yellow Fever in Uganda.** *Ann. Trop. Med. & Parasit.* 1948, Sept., v. 42, No. 2, 218–23. [12 refs.]

As the result of their previous studies of the epidemiology of yellow fever in Uganda, the authors concluded that the mosquito *Aëdes africanus* Theobald is probably the main vector which transmits the infection among the arboreal monkeys. Yellow fever virus was isolated from a mixed lot of *Aëdes* mosquitoes belonging to twelve species, including *A. africanus*, in 1944. Further large catches in 1944 and 1945 failed to yield virus. The method of investigation was then altered. Rhesus monkeys were placed on 16 platforms in different areas of the forest at the level of the canopy. The monkeys were tested for

neutralizing antibodies beforehand and at monthly intervals. Temperatures were taken daily. None of these animals contracted yellow fever. Further mosquito catches, and 33 monkeys on platforms, gave negative results in 1946. In 1947, it was found that *A. africanus* did not readily enter the type of monkey cage used, so that monkeys were then secured uncaged on 39 platforms. The monkeys all remained negative in 1947 in Bwamba where most of the platforms were, but one monkey stationed at Zika in the forest on the shore of Lake Victoria became infected and recovered. On the other hand, mosquito catches were negative in Zika but the virus was isolated in December 1947 from a batch of *A. africanus* from Bwamba. *F. O. MacCallum*

HADDOW, A. J. & DICK, G. W. A. **Catches of Biting Diptera in Uganda, with Anaesthetized Monkeys as Bait.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 271–7.

The authors continue their studies on mosquitoes in Uganda, giving particular attention to those species which live in forest canopy [this *Bulletin*, 1949, v. 46, 172]. They are much interested in *Aëdes africanus* which lives much in treetops and has been shown to contain virus.

They here describe experiments, using monkeys (*Cercopithecus* of two separate species and Indian rhesus monkey), narcotized with nembutal. They only record mosquitoes which actually bit the monkeys, which were exposed at various levels from the ground to the treetops. In each of three catches the most frequent biter was *Aëdes africanus*. It forms a higher proportion of the catch on monkey than on man (the converse being true of *Anopheles gambiae*). They record fifteen species of mosquito and one *Chrysops* biting monkeys.

P. A. Buxton

DENGUE AND ALLIED FEVERS

KAWAMURA, R., FUKUSUMI, S., ITOH, T., ITOH, H., TAKAGI, S. & OBATA, Y. Kulturelle Ergebnisse im bebrüteten Hühnerei von Dengueerreger, Rangoon Typ. [**Results obtained by the Culture of Dengue Virus (Rangoon Type) in Embryo Chicks.**] *Kitasato Arch. Exper. Med.* 1943, June, v. 20, No. 1, 1–26, 4 charts & 8 figs. on 3 pls. (2 coloured). [17 refs.]

The authors have maintained a strain of dengue virus in embryo chicks through 20 passages, and have transmitted infection to human beings by inoculation with suspensions of the chorioallantoic membranes of infected embryo chicks of the 14th passage.

Modified attacks were also produced in Formosan apes by similar suspensions of membranes of the 15th passage.

The naked-eye and microscopic changes produced in the chorioallantoic membranes are described ; in all essentials these appear to correspond to those described by SHORTT *et al.* who, in 1936, were the first to employ embryo chicks for cultivating the virus.

Round and elliptical inclusion bodies found in the mesenchyma cells of the infected membrane are described and illustrated ; their nature is regarded as doubtful. *John W. D. Megaw*

BARLOVATZ, A. Fièvre rouge congolaise et mononucléose. [**The Red Fever of the Congo and Mononucleosis.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Sept. 31, v. 28, No. 3, 315–43.

The author gives a clinical description of an epidemic of a short fever which occurred during the first half of 1948 at Yangambi on the Congo River 100 kilometres down-stream from Stanleyville.

There were 30 cases among the European population and it is stated that sometimes as many as 50 per cent. of the Europeans in certain localities of the Belgian Congo are attacked by the disease.

The disease is described as a fever with rapid onset, lasting a few days, and associated with a scarlatiniform, rarely morbilliform, rash. A variable degree of enlargement of the lymphatic glands occurs ; asthenia and rheumatic pains often persist for a long time after defervescence.

At the onset leucocytosis was usual, but in three of the nine cases in which the results of repeated blood counts are given the total leucocyte count fell rapidly ; in one case to 2,000, in another to 2,100, and in the third to 3,300 per cmm. In the later stages there was often a pronounced lymphocytosis or monocytosis. The Paul-Bunnell reaction (agglutination of sheep erythrocytes) was positive in some cases, and the author regarded the disease as being clinically related to the " infectious mononucleoses ". He admits, however, that it is not easy to differentiate the disease from dengue ; the only points mentioned being that the saddle-back temperature curve which occurs in typical dengue was hardly ever seen in the Yangambi epidemic, and that the rash appeared rather earlier than would be expected in dengue.

[Apparently the name *fièvre rouge congolaise* has been applied to several kinds of short fever, and in most cases the term P.U.O. (pyrexia of uncertain origin) would be more appropriate.] *John W. D. Megaw*

RABIES

WRIGHT, J. T. & HABEL, K. **A Comparison of Antigenicity and certain Biological Characteristics of 6 Substrains of Pasteur Fixed Rabies Virus.** *J. Immunology.* 1948, Dec., v. 60, No. 4, 503–15, 2 figs. [22 refs.]

In a previous article [this *Bulletin*, 1948, v. 45, 478] it was shown by the authors that different substrains of the original Pasteur fixed virus varied in their ability as challenge virus to produce rabies in mice equally immunized by any given vaccine, including a vaccine prepared from the homologous virus. This ability to break down a given amount of immunity—designated as the relative " invasiveness " of the viral substrains—appeared to be unrelated to the degree and breadth of the antigenicity of the substrain used as a vaccine and to its ability to produce rabies in non-immunized animals. [The substrains in question had been carried in different laboratories over a period of years by different workers using different intracerebral passage techniques.]

If, as the authors believed, this ability to break down immunity by an intracerebral challenge was an essential characteristic of the viral substrain, then it should be capable of demonstration by immunological techniques, other than the intracerebral cross-immunity type of test.

To this end, the experimental work described in the present paper was primarily devised. The nature and scope of the main investigation will be best appreciated by quoting the authors' general plan of study. "Vaccines made from each of the six substrains of the Pasteur fixed rabies virus were used in the immunization of six groups of mice. In turn, portions of each group were challenged with each of the six substrains in a cross intracerebral immunity test and a cross intramuscular immunity test. The study was planned in such a way that the vaccine and the challenge virus from each substrain was produced from a single suspension of pooled mouse brains from a single virus passage". [Such procedure precludes the criticism levelled against results previously published by certain other workers in this field, *viz.*, that many of the cross-immunity tests have not been comparable because a challenge strain used in the different tests has not been derived from a suspension of pooled brains of the same animal passage.] "Altogether there were six vaccines to be challenged by each of the six viruses. Additional mice were added to each vaccinated group for bleeding purposes. Fifteen to twenty of these mice were bled from the heart on the fourteenth day after the administration of the first of the six vaccinating doses" [0·25 ml. of irradiated vaccine containing 0·5 per cent. brain tissue, given intra-abdominally every other day]. "The blood of all mice which received the same vaccine was pooled and the serum stored without preservative at −5°C. until used for virus neutralization or complement fixation studies".

The results of intramuscular cross-immunity, cross-neutralization and cross-complement fixation confirmed those previously obtained and now repeated by the intracerebral cross immunity test, *viz.*, that ability to break down immunity ("invasiveness") is a constant and essential characteristic of the particular virus substrain.

Other experimental investigations made concurrently with (and complementary to) the immunity studies referred to above permit the authors to reach the following conclusions :—

"Substrains of Pasteur fixed rabies virus are not identical in their antigenicity, incubation period, duration of symptoms, pathology, or in their ability to overcome rabies immunity in immunized mice.

"Ability to overcome immunity would seem to be a sensitive characteristic capable of differentiating viruses of rabies of the same ancestry but of differing biological evolution and may be shown by methods of testing other than the intracerebral cross immunity test."

G. Stuart

PLAGUE

GUNNISON, J. B. & LAZARUS, A. S. **Alteration of *Pasteurella pestis* Bacteriophage following Successive Transfer on *Pasteurella pseudotuberculosis* and on Shigellae.** *Proc. Soc. Exper. Biol. & Med.* 1948, Nov., v. 69, No. 2, 294–6.

In a previous paper [see this *Bulletin*, 1947, v. 44, 1064] the authors have shown that a strain of *Pasteurella pestis* bacteriophage caused lysis of 19 out of 27 strains of *P. pseudotuberculosis*, and of 6 out of 37 strains of shigellae. They also found that after transfer on shigella the phage became more active on sensitive strains of that organism.

In the present experiments it was found that a *P. pestis* phage lysed 31 out of 40 strains of *P. pseudotuberculosis* and that after adaptation to one of these it became capable of lysing the 9 strains previously resistant to its action. This "adapted" phage after transfer on *S. dysenteriae* [*shigae*] reverted to its

original characteristics and ceased to lyse the above-mentioned 9 strains, but after further transfer on the strain of *P. pseudotuberculosis* already used it again became active against all the 40 strains of the organism.

The adapted phage when mixed with lysates of *S. dysenteriae* [*shigae*] was still active against all the 40 strains of *P. pseudotuberculosis*, and it also remained active against all of these strains after transfer on *S. paradysenteriae* [*flexneri*], *S. sonnei*, *S. ambigua* [*schmitzi*], or all of these strains. *John W. D. Megaw*

McDougall, W. A. **An Investigation of the Rat Pest Problem in Queensland Canefields: 6. Controls and Conclusions.** *Queensland J. Agric. Sci.* 1947, Dec., v. 4, No. 4, 79–139, 4 pls. & 1 fig. [43 refs.]

Blanc, G. Longue persistance de la virulence du bacille pesteux chez la puce du rat *Xenopsylla cheopis*, conservée morte à sec. **Prolonged Virulence of *Pasteurella pestis* in Dead Rat Fleas, *Xenopsylla cheopis*, preserved in the Dry State.** *Ann. Inst. Pasteur.* 1948, Dec., v. 75, No. 6, 569–571, 1 fig.

The author, with Baltazard, has already shown that *P. pestis* can maintain its virulence for as long as 16 months in the dejecta of fleas [this *Bulletin*, 1946, v. 43, 1038]: they also found that dead fleas may harbour virulent plague bacilli after 150 days' preservation in the dry state.

Blanc has now continued these latter experiments with a virulent strain of *P. pestis* maintained by flea-rodent-flea passage. Lots of the infected fleas were preserved *in vacuo* in ampoules and at varying intervals crushed suspensions in saline were inoculated subcutaneously into guineapigs. After 12, 30, 56, 100, 210, 310, 820 and 941 days, the results were positive, the guineapigs dying in 3 or 4 days. A table shows that the temperature curves of the guineapigs were closely comparable with those of control animals dying after bites or inoculation of fresh fleas.

A final test made after 986 days was negative and the author speculates, without arriving at a conclusion, as to whether this loss of infectivity was developed gradually or abruptly. He points out that the survival of *P. pestis* in dead fleas should be confirmed under natural conditions in order to judge the true epidemiological significance of the findings, especially in relation to the carriage of infected material to places far away from infected areas, as has occurred with living fleas in jute bags [this *Bulletin*, 1947, v. 44, 997].

H. J. O'D. Burke-Gaffney

Downie, G. L. **Chronic Oedema of the Leg following Bubonic Plague. A Report of Three Cases.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 132–4.

Dieke, Sally H. **Comparative Assays of Rodenticides on Wild Norway Rats. II. Acceptance.** *Proc. Soc. Exper. Biol. & Med.* 1948, Dec., v. 69, No. 3, 593–7.

"The relative efficiencies of 8 common rodenticides were determined by offering the poisons to recently trapped wild Norway rats in a standard bait (freshly ground cornmeal) under standard conditions. The voluntary consumption of baits containing sodium fluoroacetate (1080), alpha-naphthyl thiourea (ANTU), thallium sulfate and zinc phosphide resulted in complete kills at concentrations of 0·5% or lower. A sample of arsenic trioxide of relatively high toxicity required a concentration of 4% for a complete kill. All the female rats offered 5% of a good grade of fortified red squill died, but higher concentrations, and all concentrations offered to male rats, gave only

partial kills. Barium carbonate gave good but not complete kills at concentrations up to 50% while strychnine sulfate killed few rats in the range tested.

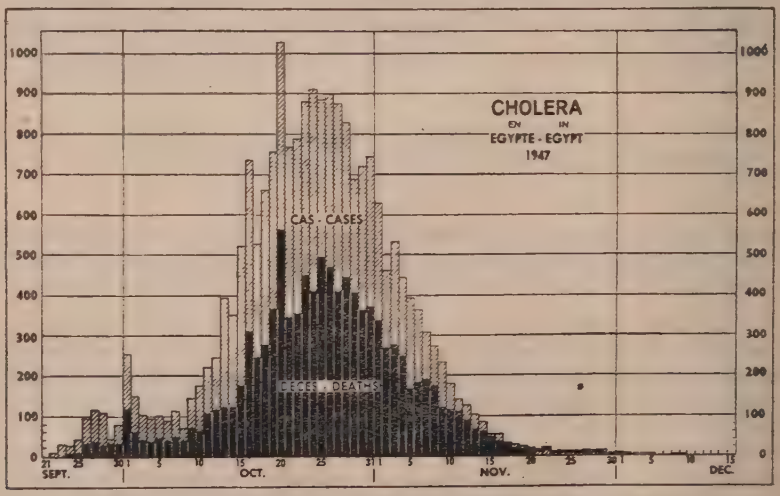
" The amounts of unpoisoned cornmeal consumed on 2 successive nights, by male and female wild Norway rats in various weight groups were determined. The addition of every poison except thallium sulfate to the cornmeal caused a considerable reduction in intake, owing either to recognition of the poison or to a rapid onset of toxic effects."

CHOLERA

SHOUSHA, A. T. **Cholera Epidemic in Egypt (1947). A Preliminary Report.** *Bull. World Health Organization.* 1948, v. 1, No. 2, 353–81, 1 map & 1 chart.

This preliminary report on the cholera epidemic in Egypt in 1947 summarizes the main features of the outbreak and the measures undertaken for its control. Egypt, which had been infected during five out of six of the great pandemics of the 19th century and had suffered severely, had been free from the disease for 45 years when cases were detected in September, 1947, at the village of El Korein in the Delta, without any warning having been given of an approaching risk, or any indication obtained from mortality statistics of a rise in incidence of epidemic disease. Immediately cholera was suspected, El Korein was cordoned off to prevent entry and exit, in the hope of limiting the spread of the disease, but almost at once cases were detected at Mostorod in the Kalyubia Province and at other points in the area.

To cope with the risk of an epidemic, special administrative and sanitary measures were immediately instituted, powers being taken by the promulgation of special decree-laws to restrict movements, to requisition supplies and to enforce sanitary and other precautions which might assist in limiting the spread of the disease. Control of traffic by rail, road and river was introduced and movement from infected to uninfected areas was prohibited except in the case



Daily cases and deaths in the cholera epidemic in Egypt (1947)
[Reproduced from the *Bulletin of the World Health Organization.*]

of persons in possession of valid certificates of inoculation with cholera vaccine. Inoculation of the crews of river craft and ferries was undertaken from the beginning of the outbreak. In spite of these precautions, cholera spread to all provinces of Lower Egypt and, although rail traffic from Lower Egypt was entirely suspended for six days to allow of the inoculation of travellers, Upper Egypt also eventually became infected.

The details of spread, in chronological order, to different parts of the country, have been published in successive issues of the Weekly Epidemiological Record of the W.H.O. [the subject has been fully reviewed in this *Bulletin*]. From the commencement of the outbreak on 22nd September to its termination at the end of November, 1947, with a few subsequent dropping cases, the total incidence recorded was 20,804 cases with 10,277 deaths giving a case mortality of about 50 per cent. The rise and fall of the epidemic is shown in the chart.

The weekly incidence by Provinces and Governorates is shown in a table (II), the highest number of cases being in the Provinces of Beheira, Gharbiya, Minufiya, Dakahliya, Sharqiya and Kalyubia in Lower Egypt. Incidence in the towns, Cairo, Alexandria, Port Said and Suez, was low.

A very brief summary is given of the measures taken. These include isolation of patients ; inoculation of contacts at the beginning of the epidemic, followed by mass inoculation of the entire population ; protection of water supplies and provision of temporary supplies ; measures to prevent infection from food and drink ; improvements in general sanitation ; and an anti-fly campaign.

To carry out the various measures applied in control and in care of the sick, a special organization was built up, the scheme for which is summarized in Table VI of the report. Members of the senior staff of the central administration were appointed to supervise the operations in each area and to arrange for staff equipment and supplies. A very large staff was placed on cholera duty, the total eventually including 930 doctors, 479 sanitary inspectors and 820 nurses.

For the early detection of cases of cholera, " flying squads " were formed to search villages and to carry out disinfection, protection of water intakes and other immediate measures. When the epidemic abated, alert measures were instituted for the purpose of detecting any persisting infection. All cases of vomiting and diarrhoea were dealt with as cholera until a bacteriological examination gave a negative result. Enquiries on all deaths were made by a medical officer of health or a sanitary inspector and swabs taken from the rectum for cultures. Out of 13,739 swabs examined between 16th December, 1947, and 12th January, 1948, positive findings were made in 43. A continuous search for carriers was undertaken.

Short notes on some of the measures taken and on the observations made are given in the report.

Protection of water supplies.—The dose of chlorine added to public water supplies was increased. Pipe lines were extended to suburbs of towns and cities and new sanitary pumps installed at villages which had not previously had pumped supplies. All Abyssinian wells (drawing water from a few feet below the surface) and open wells, were closed. Where the source of supply was from canals, sites were selected at which, only, water would be drawn and the raw water was disinfected by the addition of chlorine solution or bleaching powder.

Isolation and discharge of cases and contacts.—At first the patients were isolated in the nearest infectious diseases hospital, but as their numbers increased practically all hospitals and health centres, with the exception of one in each province which was kept for emergencies, were temporarily converted for use as cholera hospitals. Additional accommodation was later provided in tents, huts, schools or other buildings. House contacts were isolated in any available buildings and when isolation was not possible surveillance was carried out during

the incubation period. The practice adopted in regard to discharge of convalescents was to carry out a bacteriological examination of the stools on the 5th day of convalescence and again three days later. If both specimens were negative the patient was discharged, usually about the 19th to 20th day from the onset of the attack. If a positive result was reported three consecutive negative samples, at intervals of three days, were required before discharge. In the case of contacts, if two samples taken on the 2nd and 4th days of isolation were negative discharge was permitted. If one sample was positive three consecutive negatives, as in the case of convalescents, were necessary. A five-day course of sulphaguanidine was given to both convalescents and contacts while under observation, and repeated if the vibrio could still be isolated.

Duration of the "carrier" state.—Observations were made on the period of persistence of the vibrio in the stools of 463 convalescents in four hospitals. The findings are shown in Table X of the report. The minimum and maximum periods from the beginning of the attack at which the vibrio was isolated are stated to be respectively 7 and 42 days. A considerable difference is shown in the table on the findings in the four hospitals. In Cairo and Alexandria respectively only 14 per cent. and 5·2 per cent. were positive after the 15th day, while in Zagazig and Tanta the figures were 31 per cent. and 76·2 per cent. respectively.

Positive cultures were obtained from 288 out of 13,702 contacts examined, giving a rate of 2·1 per cent. Of these 95 developed the disease, *i.e.*, 0·6 per cent. of total number of contacts. Table XIII of the report shows the duration of excretion of the vibrio by contacts. The majority were negative after 5 days and 93·6 per cent. were negative after 10 days. The maximum period observed was 19 days.

Observations made on the effect of sulphaguanidine and sulphacetamide on the persistence of the vibrio (Table XI) favour the use of the former drug.

The bacteriological work carried out during the epidemic involved the examination of 119,079 specimens.

Viability of V. cholerae.—Investigations were carried out on the periods of survival of *V. cholerae* on different foods and materials contaminated in one set of experiments with faecal material and with cultures in another. The results are summarized in a table. The food-stuffs tested were onion, garlic, orange, lemon, grapes, dates, lentils, rice, sugar and bread. The other articles were coins, postage stamps, bank notes and cloth. The vibrio was not recovered later than the third day on any of the food-stuffs or materials when fresh stool material was used. Survival in acid fruits such as lemons and oranges was a matter of a few hours only. The findings are tabulated.

Inoculation.—Inoculation of the whole population with cholera vaccine was undertaken. At the outset of the epidemic only a small stock, required for the inoculation of pilgrims, was in hand and it became necessary to supplement local manufacture by obtaining supplies urgently from other countries. Over 5 million ml were received as donations and 10 million ml on payment. Later the production at the Vaccine and Serum Institute in Cairo was stepped up from 40,000 ml daily to 400,000 ml to meet all requirements. The dose employed in the mass inoculation campaign was 1 ml containing 8,000 million vibrios. Staff working on cholera were given two doses, 0·5 ml followed by 1·0 ml one week later. A complete re-inoculation of the population was undertaken commencing on 15th February, 1948, as a precaution against recurrence of cholera.

In discussing the evidence on the value of inoculation the opinion is expressed that "While it is difficult to believe that vaccination alone accounts for the complete suppression of the epidemic, there is no doubt that it was of great importance in modifying the general trend of the outbreak and in reducing

incidence and mortality. The findings suggest that the epidemic of cholera was finally ended by large-scale vaccination." A comparison is made between the incidence and the fatality rate in the 1947 epidemic as compared with that of 1902, when the population was only half that of the present time. The gross morbidity rate is estimated to have been four times less in the recent outbreak and the mortality rate seven times less than in 1902, when no vaccination was undertaken. The figures of eight different fever hospitals show that 18·7 per cent. of the cases were in inoculated persons, 81·1 per cent. in the uninoculated, the case mortalities in the two groups being 26·5 per cent. and 42·9 per cent., respectively.

Antifly campaign.—In view of the possible risk of carriage of infection by flies a vigorous anti-fly campaign was undertaken in which the Insect Eradication Section and the Malaria Section of the Ministry of Public Health were employed. Aircraft were used for the purpose, "fogging" being carried out with a 20 per cent. solution of DDT in Velsical, and "spraying" with a 10 per cent. solution in kerosene. A 7 per cent. solution of DDT in Malariol was also used for ground fogging by discharge from the exhaust of a jeep. Hand-guns and mechanical pumps were used inside houses. A special evaluation of the results was undertaken by the staff of the Insect Eradication Section and a general decrease in fly population is claimed in treated villages as compared with controls. A separate report on the findings will be published.

Quarantine restrictions.—Under the heading "Cholera Hysteria," the author refers to the restrictive measures applied by certain countries against the risk of the introduction of cholera infection, which far exceeded the provisions of the International Sanitary Conventions. These included, in some cases, the complete closure of frontiers against passengers and goods, and even mail, from Egypt. One country prohibited the importation of food-stuffs, not only from Egypt, but also from eight countries "threatened" with cholera. "Other countries prohibited not only food-stuffs, but also Egyptian cotton, forgetting the fact that they had been importing for years jute from Bengal and rice from China and Indo-China, the main endemic and epidemic centres of cholera, without any evil consequence." "International control as provided for in the conventions, ought not to be set at naught and disregarded on the principle of each country for itself." Comment is made on the importance of developing a long-term policy of sanitary improvement in the known endemic areas of cholera, for the purpose of reducing the risk of spread or even eliminating infection altogether.

In concluding the report, acknowledgment is made of the generous help given to Egypt by States and private organizations during the epidemic and to the assistance rendered by the World Health Organization.

This preliminary report will form a useful background to more extended publication on the various aspects of cholera as seen in Egypt and on the observations made. *J. Taylor*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

SPINGARN, C. L. & EDELMAN, M. H. **The Use of Streptomycin in the Cultivation of *Endameba histolytica* from Stools.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 825–9.

It is difficult to grow *Entamoeba histolytica* successfully from stools containing cysts alone. If streptomycin is added to the culture medium much better results can be obtained, even from stools a week old. Three drops of faecal suspension are added to the mixture of horse-serum and saline covering the

solid slope [this *Bulletin*, 1948, v. 45, 428]. Streptomycin in varying concentrations (1 to 10 mgm. per cc.) is also added ; there is no optimum dose, because each strain behaves differently.

Control tubes without the antibiotic were set up and inoculated. Positive cultures were obtained in 8 per cent. of the controls and in 73 per cent. of the streptomycin tubes. The growth of *Blastocystis* and of bacteria was much inhibited in the latter ; trophozoites of the amoeba were usually abundant and subculture was easy. Excystation occurred within 48 hours at 37°C. but might be delayed for nine days.

The employment of a standardized technique should prove useful in the numerous cases where amoebiasis is suspected, but the diagnosis is not completely established. *P. C. C. Garnham*

CHANG, K., TONG, W. K., CHIN, H. T. & LI, C. H. *Endamoeba histolytica* **and other Intestinal Protozoa in Szechwan. A Preliminary Report.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 134–8. [10 refs.]

TRIPODI, M. Le forme a tipo setticemico dell'amebiasi. [**Amoebiasis with Septicaemic Type of Symptoms.**] *Boll. Sanitario d. Tripolitania.* 1948, July–Dec., v. 6, Nos. 3/4, 17–21. [11 refs.] English summary (6 lines).

Many patients with *E. histolytica* appear to enjoy perfect health ; others may show symptoms who have never suffered from dysentery, but become alarmingly ill with symptoms pointing to involvement of other organs, for example, liver, lungs, brain. Some cases resemble typhoid, or malaria, or undulant fever or appendicitis. In others there may be no localizing symptoms, but fever, remittent or intermittent, with sweats, shiverings, slight enlargement of the spleen, Widal negative, leucocytes not increased, 6,000–8,000 per cmm.

Three such cases are detailed. For a time they were very puzzling, but examination revealed that the patients were passing *E. histolytica* or its cysts, or both. Treatment with emetine was started. Improvement was seen in one patient, a lad of 17 years, after the first injection ; the others lost their fever in 3 days and progressed uninterruptedly to recovery. The author postulates that the amoebae may settle in some focus without producing symptoms, or that there may be, temporarily at least, immunity to their presence in the intestine, that this breaks down and a septicaemic condition—an amoebiaemia—be set up. *H. Harold Scott*

COXON, R. V. **Some Observations on Amoebic Dysentery.** *J. Roy. Army Med. Corps.* 1948, Dec., v. 91, No. 6, 243–56. [17 refs.]

The material for this paper was collected in India during 1943 and 1944. All cases were considered primary and all in the control series had lesions demonstrable sigmoidoscopically.

Emetine (0·065 gm.) was administered by deep subcutaneous injection ; emetine-bismuth-iodide was given orally as a powder derived from crushing a tablet preparation, the daily dose (0·2 gm.) being taken in the evening. In the majority of cases, the first dose induced a marked degree of nausea which was taken to imply that it was being satisfactorily absorbed. For quinoxyl retention enemata 250 ml. of a 2·5 per cent. (w/v) solution in water were used. The enema was preceded by a wash-out with 2·0 per cent. aqueous sodium bicarbonate solution with the patient lying on the left side and afterwards adopting the knee-elbow position. A series of 9 cases receiving no special treatment saving retention enemata of saline were retained as controls.

Amibiarson (Martindale, 1941) was given by mouth in form of tablets, the dose being 0·25 gm. morning and evening. Oral quinoxyl was in aqueous solution : two doses, each containing 0·25 gm., were given daily.

Test of Cure.—Specimens of 6 stools passed at intervals of not less than twenty-four hours were examined for trophozoites and cysts of *E. histolytica.* Sigmoidoscopy being negative the patient was transferred to the Convalescent Depot for 3 weeks where he lived on normal Army rations. At the conclusion three further specimens of faeces were examined and another sigmoidoscopy was made.

A case was recorded as a " success " if, at the conclusion of this period, no evidence of recurrence had been obtained.

The schedules of treatment are shown in a table and are divided into 5 groups :

1. Emetine, 0·065 gm. daily, 1st to 6th day ; E.B.I., 0·2 gm. daily, 7th to 12th day and 20th to 25th day ; quinoxyl rectally, 5th to 14th days : amibiarson, 0·25 gm. twice daily, 13th to 25th day.
2. E.B.I. 0·2 gm. daily and quinoxyl rectally, 1st to 10th day ; quinoxyl 0·25 gm. twice daily, for one month.
3. Emetine, 0·065 gm. daily, 1st to 6th day and 10th to 15th day ; amibiarson, 0·25 gm. twice daily, 7th to 16th day.
4. E.B.I. 0·2 gm. daily, 1st to 11th day.
5. (Control). Distilled water, 1 ml., 1st to 6th day ; sodium bicarbonate 0·5 gm., 7th to 12th day and 20th to 24th day ; rectal saline, 5th to 14th day ; glucose, 1 gm. twice daily, 13th to 25th day.

The successes for each of the first four groups are shown respectively as 91·7, 72·7, 92·3 and 80 per cent. (average, 84·8) : for the control group, the successes are shown as 22·3 per cent.

Concomitant bacillary infection was discovered in nine cases and sulphaguanidine was considered to be indicated only when frequency of defaecation was exhausting or there was severe tenesmus. On several occasions amoebae were seen moving among cells of a typical " bacillary exudate."

In the control series of 6 cases receiving no specific treatment, the ulcers which had been visualized through the sigmoidoscope disappeared within periods varying from ten to twenty-four days.

It is concluded that reasonably satisfactory results could be achieved by either oral E.B.I. or parenteral emetine combined with an organic arsenical, but no appreciable improvement resulted from the addition of quinoxyl retention enemata, while sigmoidoscopic observation of control cases showed healing of amoebic ulcers in absence of specific medication. *P. Manson-Bahr*

GIMBLE, A. I., DAVISON, C. & SMITH, P. K. **Studies on the Toxicity, Distribution and Excretion of Emetine.** *J. Pharm. & Exper. Therap.* 1948, Dec., v. 94, No. 4, 431–8, 4 figs. [10 refs.]

In this investigation on the toxicity and metabolism of emetine in animals, two methods were used for estimation. The first, described by BRODIE *et al.* [this *Bulletin*, 1947, v. 44, 793], in which methyl orange is the reactant, can be used generally for organic bases but is not specific. By washing the ethylene dichloride tissue extract with phosphate buffer at *p*H 7·5 the method gave greater specificity and increased accuracy. Before extraction, the protein to which emetine is firmly bound was precipitated with trichloracetic acid. The colour developed was read in a spectrophotometer at 540 mμ and then compared with standards. In a second method, use was made of the ultraviolet absorption curve of emetine as determined in a Beckman spectrophotometer. Details of the procedure should be consulted in the original.

Acute toxicity was determined in rats and mice by intraperitoneal injection. The LD_{50} in mice was 62 mgm. per kilo. and in rats 17 mgm. per kilo. After administration of 40 mgm. emetine per kilo. to groups of mice, the drug content of the whole animal was determined at intervals up to 35 days. The amount present decreased till the 8th day when approximately 35 per cent. of the administered dose remained in the body, and was approximately the same in amount until the 35th day, indicating that the drug was slowly disposed of. These observations are in agreement with the fact that repeated small doses prove as toxic to animals as a single large dose. When the above dose was doubled the residual drug in the body was the same as above, so that above a certain storage level emetine appears to be excreted or destroyed. Distribution in the different tissues of rat and dog showed that most was stored in the liver, and may explain the drug's effectiveness in amoebic abscess of that organ. Smaller amounts were present in kidney, spleen, lung, brain, heart, muscle and blood in that order. The small amount present in heart was surprising since it exerts marked toxic effects on this organ. Urinary excretion alone was studied in the same animals and one human patient. Only traces of emetine could be found in a 24-hour sample and the drug was evidently not excreted to an appreciable extent by that route. *J. D. Fulton*

i. RICKARDS, A. G. **The Treatment of Amoebiasis with "Diodoquin".** *J. Trop. Med. & Hyg.* 1949, Feb., v. 52, No. 2, 33–8. [14 refs.]

ii. J. TROP. MED. & HYG. 1949, Feb., v. 52, No. 2, 23–4. **The Cyst-Passer again.**

i. This survey includes the treatment of 127 consecutive cases of amoebiasis of all grades treated with diodoquin. In all, ambulant treatment was adopted. The post-therapeutic supervision proved difficult as the men were demobilized a month after therapy was finished and all faeces examinations thereafter had to be undertaken on specimens sent by post.

The criteria of cure consisted in the remission of symptoms and examination of not less than 6 faecal specimens within a period of not less than three months after cessation of therapy.

The series was grouped into :—

Group I. Asymptomatic.
Group II. Asymptomatic with visible lesions on sigmoidoscopy.
Group III. Symptomatic with no bowel lesions on sigmoidoscopy.
Group IV. Symptomatic with bowel lesions on sigmoidoscopy.

121 fell into the first three groups : 96 were in Group I, 7 in Group II and 18 Group III.

As the first three belong to the non-dysenteric type they may be considered together. Of these 121, 90 were classed as "cures", 16 as failures, and 15 as having insufficient data.

The highest relapse rate (25 per cent.) occurred among those treated by an eight-day course of diodoquin. This rate was reduced to 10 per cent. among those receiving a fourteen-day course and to nil among those receiving a twenty-one-day course of therapy. Patients in Group IV were most unsatisfactory. All cases came from India and there was only one cure. In three diodoquin treatment was combined with E.B.I. Regarding toxicity the high iodine content of diodoquin presages a greater potential danger of toxicity than does vioform.

In the present series of 127 cases, only 16 instances of untoward effects after administration of the drug were encountered. Pruritus ani was the most prominent, but was never a serious contraindication. Headache was not a prominent feature.

The disappearance of *Entamoeba histolytica* from the faeces showed a marked constancy in the first three groups and in only two could cysts be found five days after therapy was begun, but the interval of disappearance was longer in the last group of cases. *E. coli* and *I. bütschlii* were quickly eradicated, but *Giardia intestinalis* and *Endolimax nana* were resistant.

The usual dosage in the first three groups was 9 tablets (28·8 grains) *per diem*. From the results of treatment among the first three groups it is clear that there is a marked reduction in the relapse rate in those men treated for a longer period. It appears that less than twenty days treatment must be considered inadequate.

The maximum dosage was 1,123·2 grains (351 tablets) given within thirty-five days and no untoward reactions were produced.

The response to treatment was more marked in the acute forms of the disease when complete relief from symptoms was often obtained. One patient gained 7½ lb. in weight within fifteen days and all the remaining cases showed such an initial dramatic clinical improvement. Sigmoidoscopic appearances ran a parallel course.

The earlier American reports of the efficacy of diodoquin have not been confirmed, but there is no doubt that it is a useful addition to the list of amoebicidal drugs, and the main indication lies in the treatment of the symptomless cyst-passer on account of its low toxicity.

It should, however, never be used alone in the treatment of amoebic dysentery, but is of real value when used in combination with emetine compounds.

ii. In an editorial commenting on this paper and a previous one by the same author [this *Bulletin*, 1949, v. 46, 361], reference is made to the problem of the cyst-passer and the significance of asymptomatic ex-servicemen returning to the community. The greater incidence and far greater morbidity from *E. histolytica* infection in this series among men returning from the India-Burma area, as compared with those from the Mediterranean, is discussed : and it is suggested that some local factor is involved and that, perhaps, such a factor is absent altogether in temperate countries. *P. Manson-Bahr*

LAVIER, CROSNIER & MERLE. Traitement de l'amibiase par la conessine. [**Treatment of Amoebiasis with Conessine.**] *Rev. Paludisme et Méd. Trop.* 1949, Jan. 15, v. 7, No. 56, 1–8.

The authors, and other French workers, have already recorded satisfactory results in the treatment of amoebiasis with conessine [this *Bulletin*, 1948, v. 45, 905 and 1086]. With further experience of it they confirm their view that conessine is the equal of emetine, not only in the treatment of intestinal amoebiasis but in that of acute amoebic hepatitis. The drug is well tolerated by young patients, and with habituation by others, though sedation is necessary in some cases. *A. R. D. Adams*

LARSH, J. E., Jr. & CHAFFEE, E. F. **The Effectiveness of Carbarsone in rendering Young Mice Free of Intestinal Protozoa.** *Science.* 1948, Dec. 24, 725.

The common laboratory rodents are naturally infected with amoebae and attention has been drawn to this fact in connexion with the use of rats as experimental hosts for *E. histolytica* by FULTON & JOYNER [this *Bulletin* 1948, v. 45, 430]. The present authors have attempted to free mice, kept under controlled conditions, from intestinal protozoa, by means of carbarsone. Groups of animals which received 50 to 300 mgm. of the drug daily per kilo. by mouth

for 10 days were not rendered protozoa-free by this treatment. Doses up to 1,500 mgm. per kilo. proved effective in reducing their numbers but failed to eradicate them. *J. D. Fulton*

NEAL, R. A. *Entamoeba muris* : **a Complicating Factor in the Experimental Infection of Rats with** *E. histolytica*. [Correspondence.] *Nature*. 1949, Jan. 15, 99–100, 2 figs.

As recently pointed out by FULTON & JOYNER [this *Bulletin*, 1948, v. 45, 430] the presence of natural amoebic infections in rodents used for experimental infection with *E. histolytica* may give rise to difficulty in interpretation of the results obtained. The present author indicates that infection with *E. muris* may be avoided by selection and care in maintenance of animals used. The effect of emetine and carbarsone on young rats experimentally infected with *E. muris*, through giving mature cysts in food, has been determined. Treatment by the drug-diet method was begun immediately after giving the infection and lasted for 6 days. The drugs proved ineffective against *E. muris*, as was found by HEGNER & ESKRIDGE (*J. Parasitology*, 1936, v. 22, 408). Some morphological descriptions of the rat parasite are added. *J. D. Fulton*

GERUNDO, M. **Control of Hepatic Coccidiosis of Rabbits with Succinylsulfathiazole U.S.P. A Study of the Mode of Action of the Sulfonamides.** *Arch. Pathology*. 1948, Aug., v. 46, No. 2, 128–31.

RELAPSING FEVER AND OTHER SPIROCHAETOSES

GAMBLES, R. M. & COGHILL, N. F. **Relapsing Fever in Cyprus.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 288–303, 1 map. [35 refs.]

Relapsing fever has probably been endemic in Cyprus for many years but was not diagnosed until 1939, when spirochaetes were found in the blood of two gold miners suffering from fever. Between 1941 and 1943, 98 soldiers contracted the disease and cases also occurred amongst the civilian population. The origin of some of these cases was discovered by WOOD & DIXON [this *Bulletin*, 1946, v. 43, 44] ; they noted that the soldiers had been using caves or dungeons containing the tick *Ornithodorus tholozani*. The present authors extended these observations and discovered that the disease was widespread in Cyprus. Clinically the cases did not resemble the louse-borne form and most of the patients were later proved to have been in contact with ticks. One of such ticks was sent to ADLER, who was able to prove that it was infected with spirochaetes. Other transmission experiments with ticks were negative.

O. tholozani was found in nine different sites in Cyprus. Never found in human habitations, the ticks occupied caves, rock shelters and once a ruined church. The ticks live in the dry earth or sand on the floor of the caves, in rat-holes, or even in the earth at the base of a cliff below the cave. The ticks appear to flourish particularly where the floor is inches deep in guano. Infection takes place not only in people sheltering or sleeping in the caves, but also in those merely visiting and crawling about in them. The species of tick is active in its movements, attacking the legs and ankles and remaining in the clothing after engorgement. The ticks probably feed on rodents ; man is only an accidental host. The rôle of rodents as reservoirs of spirochaetes was investigated by examining the blood of 10 black rats and one spiny-mouse from places known to be infected with the disease. The brains of nine of the rats were also inoculated into guineapigs. All the results were negative. Ticks were kept alive unfed for as long as 480 days. *P. C. C. Garnham*

ASHBEL, R. **Notes on *Spirochaeta persica* from Palestine and Spirochaetes of Relapsing Fever from the Western Desert (Tobruk Area).** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan , v. 42, No. 4, 409–10.

A summary of observations on thirteen strains of spirochaetes isolated from twelve patients and one tick (*Ornithodorus tholozani*) at Tobruk, and a comparison with strains of *Spirochaeta persica* from Palestine The cases of relapsing fever occurred among soldiers in the Western Desert and the strains were supplied by Col. Boyd and Lt. Col. Little, G.H.Q., Middle East Command.

Guineapigs were found to be highly susceptible to 11 of the Tobruk strains but resistant to two of them. After intraperitoneal injection the incubation period in guineapigs varied from 2 to 10 days, and there was no uniformity in the course of the infection. Some of the animals showed a heavy infection lasting about a fortnight, without any relapse, while others had 3 and 4 relapses in the space of 2 or 3 weeks, and one individual even 5 relapses.

In the case of the Palestine strains, an animal can be considered to have recovered when its blood remains negative for one month, but Tobruk strains can still be transmitted by the inoculation of heart blood 10 months after the disappearance of spirochaetes in thick drop examinations. In both strains the brain remains infective after the blood has become negative. In the case of the Palestine strains the brain has been shown to be infected 20 months longer than the blood in rats, and more than a year longer in guineapigs. The total period of brain infectivity with Tobruk spirochaetes has not yet been ascertained.

Guineapigs which have recovered from infection with Palestine strains remain immune to the same strains. In the case of the Tobruk strains some animals develop specific immunity, while others do not ; and in the latter cases a second infection with the same strain produces an infection equally as heavy as the first. On the contrary, an animal infected with the Palestine strain, if inoculated with a new strain, develops an attack less severe than the previous one. It was noticed in Tobruk strains that the longer the incubation period in an animal, the more severely does it become infected, and some of these animals died with haemorrhages in the lungs, liver, peritoneum and brain.

Ornithodorus tholozani was shown to be capable of transmitting the Tobruk strains by bite. The contents of lice fed on monkeys infected with Tobruk strains remained infective to guineapigs for a maximum period of 48 hours.

E. Hindle

HEISCH, R. B. **The Human Louse in Transmission of *T. duttoni* in Nature.** *Brit. Med. J.* 1949, Jan. 1, 17.

It had been previously shown [this *Bulletin*, 1948, v. 45, 603] that the human louse could act as a vector of *Treponema duttoni* in the laboratory. This organism is normally carried by *Ornithodorus* ticks ; now the author has shown that it can develop in lice recovered from patients suffering from the *duttoni* form of relapsing fever.

Lice were collected from the clothes of patients ; they were kept for periods up to three days and were then inoculated into susceptible animals. The animals became infected with a spirochaete which showed the typical characters of *T. duttoni*. It seems probable that the louse may therefore be a natural vector of the disease, though why epidemics of louse-borne *T. duttoni* do not occur remains a mystery.

P. C. C. Garnham

YANG, R. Y. & TU, Sou-chao. **Treatment of Relapsing Fever at the Chengtu General Hospital.** *Chinese Med. J.* 1948, Aug., v. 66, No. 8, 426–30.

" 1. The results of treatment of 79 proved cases of relapsing fever in the Chengtu General Hospital from 1942 to 1944 were presented.

"2. Thirty-eight cases treated with arsenic preparations 3–4 days after the crisis of the first attack showed no relapse after 12–20 days observation following injection except one case treated with mapharsen.

"3. Of 40 cases treated before crisis, relapse occurred in 7 with one death.

"4. Phenarsine hydrochloride was found to be as effective as neo-arsphenamine but caused more reaction."

YAWS

HACKETT, C. J. **The Bone Lesions of Yaws in Uganda. A Clinical and Radiological Study.** [Thesis presented to the University of London for the Ph.D. degree in the Faculty of Medicine, November, 1947.] Typewritten MSS. 262 pp., 1 map, 2 graphs & 133 photographic figs. [43 refs.]

This work records an extensive radiological and clinical study of bone lesions in yaws carried out from 1937–40 while the author was holding a Senior Fellowship in Tropical Medicine of the Medical Research Council. Two visits were made to the Lango district of Uganda. During the first visit, 340 cases of yaws with bone lesions were studied and 220 patients were re-examined during the second visit a year later. The period of observation of individual patients ranged from 6 to 18 months, and some 3,000 X-ray and 5,000 clinical photographs were made.

The Lango area just north of the equator, is low, undulating savanna country interspersed with swamps. It has an average rainfall of about 57 inches falling in two periods with maxima in May and August. The Lango tribe was pastoral but is becoming agricultural. The diet is largely vegetarian and probably poor in animal protein and fat ; infants are breast-fed for one to two years. Young children are usually naked but adults wear simple clothes.

That the bone lesions described in this work were indeed due to yaws seems beyond question for the following reasons. The majority of the patients had generalized yaws lesions or had a history of such lesions. The bone changes formed a connected whole such as may be expected from a single aetiological agent, and they resolved after treatment with neo-arsphenamine. Syphilis appeared to be so rare that it could be excluded as a cause of the widespread bone lesions, and for the purpose of this study, yaws and syphilis are regarded as two different diseases ; in Lango, yaws is common (among the 14,000 average annual out-patients 20 per cent. show evidence of yaws), and typical syphilis is rare, whereas the opposite obtained at Masaka. The nature and sites of the lesions excluded tuberculosis or leprosy as the specific cause of the bone changes. Nutritional deficiencies may predispose yaws patients to the development of bone lesions but there was no evidence that such deficiencies in themselves accounted for the lesions.

Classification of yaws

Secondary lesions resemble the initial.

Generalized secondary lesions have a granular appearance and spirochaetes are readily demonstrable in serum from the lesions ; these lesions are never destructive and leave insignificant scars on healing.

Later, destructive ulcerations develop which, on healing, leave thin, shiny, deeply pigmented, atrophic scars ; lesions of this type are never present at the same time as secondary lesions nor do secondary lesions develop into them. These are tertiary lesions and spirochaetes are rarely found in them.

Latent secondary cases are those without skin lesions but whose bone lesions resemble those usually found with secondary lesions ; sometimes typical secondary skin lesions develop later.

Similarly latent tertiary cases are those without skin lesions but whose bone lesions resemble those of tertiary cases.

Secondary lesions cease to relapse within a few years after infection. Tertiary lesions develop some years after infection and follow a symptom-free period. At any stage the disease may become inactive.

Bone lesions in the various stages of yaws

Secondary cases.—Among 169 secondary cases (167 with skin lesions and 2 in the "pre-secondary stage") 20 per cent. were under 2 years of age and 70 per cent. below 5 years of age; 108 patients complained of bone pains, often nocturnal; 123 had thickening of bones with tenderness; 100 had the initial lesion or its scar; all had some type of skin lesion. From examinations of the patients 6 to 18 months later, it appeared that active bone lesions were nearly twice as frequent in patients with relapsed skin lesions as in those with resolved skin lesions. Younger patients suffered relapses of skin lesions more frequently than older ones. It appeared that the younger the patient, the shorter the duration of the yaws, and the less numerous the neo-arsphenamine or bismuth injections, the greater was the tendency of the skin lesions to relapse.

The majority of bone lesions commenced during the first or subsequent generalized skin eruptions. All active bone lesions tended to resolve spontaneously after a few weeks or months, but treatment hastened healing. No ulceration of bone lesions through skin or spontaneous fracture was seen.

The radiographic appearances indicated active changes (rarefactions: periosteal deposits), and inactive changes (cortical thickening and bony expansion; sabre-tibia); combinations of these changes occurred. Sabre-tibia was probably due to periosteal deposits which had become organized on to the anterior surface of the cortex and increased its convexity; there was no evidence that yaws played an important part in producing bowing of the tibial shaft.

Of the bones radiographed the ulna was probably most frequently involved; next in frequency were the hand bones, tibia and fibula, and lastly the foot bones and radius. In the hands and feet usually many bones were affected but the terminal phalanges, carpus and tarsus were unchanged. Apart from goundou, no clinical evidence was found of involvement of the skull, ribs or vertebral column; and radiographically no changes were found in joints, although free fluid was occasionally present in the knee joints.

The periosteal deposits indicate active periostitis, and the cortical rarefactions a rarefying osteitis; cortical and periosteal rarefaction and periosteal deposits can be regarded as an osteoperiostitis. Cancellous tissue rarefaction which was occasionally observed in young children, probably indicates localized metaphyseal osteomyelitis.

There were 15 patients, 12 males and 3 females, with granulomatous plantar yaws; three with active bone lesions were under 8 years of age, while more of the other cases were over 15 years of age than under. Most had had yaws some years before and all complained of pains in the bones, or in the plantar lesions. Absence of radiological evidence of bone lesions in some patients with bone pain was probably due to the changes being insufficiently gross. Most of the patients showed bone changes that could well be attributed to previous secondary lesions, and the active bone lesions were comparable with those seen in secondary cases.

Latent Secondary Cases.—There were 65 patients with no secondary yaws skin lesions but who were considered to be in a latent secondary stage. Of these, 18 had periosteal deposits only, 31 had cortical rarefactions and periosteal deposits, while of the remaining 16, 4 had cortical thickening and expansion,

3 organizing periosteal deposits, 4 inactive sabre-tibia, and 5 no bony abnormality. Fourteen of the first group of 18 patients were under 10 years of age and most had had yaws a year or more previously. Pain in thickened bones was the most frequent complaint ; many of the bones showed the results of earlier secondary yaws lesions, *i.e.*, thickening and expansion and added to these were periosteal deposits similar to those seen in other secondary cases. One case when seen later had developed a further eruption of secondary skin yaws.

Twenty-three of the second group of 31 patients were 10 years of age or under, and in most cases yaws had been contracted some years previously All complained of bone pain and had tender bony thickenings. The cortical rarefaction and periosteal deposits observed and the changes that occurred on resolution were comparable with those in the secondary cases, although minor differences were observed, and bony expansion and cortical thickening were more frequent.

All patients of the third group of 16 had yaws a year or more previously, and most of them complained of bone pain. Their ages ranged from 4 to 20 years, but 13 were between 6 and 18 years of age. In 5 cases no bony changes were present and 4 had sabre-tibiae ; the changes in the other cases were comparable with those seen in other secondary cases. One case 19 months after the first observation had secondary palmar and plantar yaws.

Tertiary Cases.—One hundred and nineteen patients were regarded as having tertiary lesions. Radiologically they fell into 4 groups ; 13 with small well-defined cortical rarefied foci, 48 with large well-defined cortical rarefied foci, 28 with ill-defined cortical foci, and the remaining 30 patients.

Of the first group of 13 patients, 9 were over 15 years of age, and all had had yaws some years before. All complained of pain, and in 7 the duration of this symptom was 9 months or over. Tender bony swellings or nodes were present in all patients, together with small (1–3 mm. diameter) cortical rarefactions. In two cases, tertiary yaws skin ulcerations were present, and in one ulceration through the skin from a bone lesion occurred.

Of the second group of 48 patients, 17 were 10 years of age or under, while 19 were over 15 years. All had had yaws, in most cases several years previously, and all complained of pain, mainly in thickened and tender bones. In 18 patients the duration of the complaint was six months or less, and in 20 over one year. Nodes on the skull and tertiary yaws ulceration were present in some cases. The tibia, ulna and radius were most frequently affected. The radiographic appearances consisted of moderately well-defined rarefied foci (5 mm. diam.) in localized or extensive cortical thickening and expansion. Probably the earliest changes were rarefied foci in the cortex. Periosteal deposits then appeared and became organized ; into these deposits the foci extended or in them some other foci appeared. On resolution periosteal deposits and rarefied foci disappeared and the expansion and cortical thickenings were reduced, although usually some expansion and thickening remained. During the height of activity in some cases ulceration occurred from the bone lesions through the skin. In many patients seen several months to a year after the first observation, the bone lesions had resolved but in some they had persisted, relapsed, or more recent lesions had appeared. In many cases the tibiae were bowed, but no increase in this deformity was observed during the period of observation. In one patient there were gross lesions of the hip joint, and in a few there were rarefied areas in the epiphyses or metaphyses. No spontaneous fracture of long bones was observed.

Of the third group of 28 patients, 2 were 10 years of age or under, and 20 were over 15 years of age. All had had yaws, in most cases for a number of years, and all complained of pain, usually in thickened and tender bones. In over half the cases the duration of the complaint was 6 months or less, and in nearly a

third it was a year or more. Tertiary skin lesions were present in some cases. In the radiographs, large ill-defined foci of rarefaction were found in the cortex which was often thickened; the changes were localized rather than generalized. The evolution of the lesions resembled that of the cases with large well-defined rarefied foci. Ulceration of bone lesions was also observed. In many patients the tibiae were bowed, but no alteration in this was found during the period of observation. In two cases there were destructive lesions of the articular surfaces of the elbow and knee. In one case there was ankylosis of the elbow and in another spontaneous fractures occurred in the ulna.

In the remaining group of 30 patients, one was 7 years of age and 26 were over 15 years. All had had yaws some years previously and all complained of pain in bones or skin lesions; in a number tertiary skin lesions were also observed. In the radiographs a variety of changes were present, including rarefactions, periosteal deposits, cortical thickening and arthritis. In two patients with hydrarthrosis and in three with tertiary skin ulceration, no change was found in the bones.

The characteristics of tertiary lesions in the hand bones were the relatively few bones involved and the destruction that often occurred; carpal bones were sometimes involved. Sinus formation, spontaneous fracture, shortening and deformity often developed, and some lesions were of long duration. The changes in the bones of the foot resembled those of the hand but were probably less frequent. The tertiary lesions in the skull comprised gangosa and areas of rarefaction in the normal or thickened cortex of the outer table of the calvarium. The cortical rarefactions were associated with fluctuant swellings which might undergo absorption or ulceration.

In tertiary cases, the periosteal deposits may be regarded as evidence of periostitis, and the rarefactions indicate localized areas of osteitis. Bony expansion and cortical thickening result from periosteal activity depositing bone on the surface of the cortex. In brief the radiographic appearances indicate a focal destructive inflammatory reaction of the various tissues of bone. Some lesions were more diffuse and less destructive.

It was noted that non-yaws ulceration was not associated with rarefied foci in underlying bones, although periosteal deposits and cortical thickening might be present. Slightly bowed tibiae were found in some patients who probably had not had yaws.

Summarizing the radiographic findings, secondary cases showed focal rarefactions in the cortex, and periosteal deposits in which rarefactions also occurred. As resolution proceeded, the rarefactions usually cleared up before the periosteal deposits were absorbed or became organized on to the surface of the cortex. Although in many lesions the bones finally returned nearly to normal appearance, cortical thickening and bone expansion sometimes resulted. In the tibia such changes might lead to increased convexity of its anterior profile (sabre-tibia) although actual bowing of the tibia is probably due to some factor other than yaws, possibly nutritional. In secondary bone lesions and, to a less extent, in tertiary lesions, spontaneous resolution in a few months was the rule, but healing was hastened by specific therapy.

Secondary bone lesions were not destructive, but recurrence of activity was not infrequent after apparent resolution. The dactylitis of this stage involved many of the metacarpals and phalanges, but the distal phalanges, carpus and tarsus were not affected. Often many long bones were involved. Spontaneous fractures, lesions of the skull except goundou, ribs and joints and ulceration of bone lesions through the skin were not observed. No change resembling active rickets or syphilitic osteochondritis was found.

In tertiary cases the main changes were small (1–3 mm.) and large (5–10 mm.) well-defined rarefied foci, and ill-defined foci (10–20 mm.), in the cortex which

might or might not be thickened. Lesions were more localized than those in secondary cases. The rarefied foci were single or multiple, discrete or confluent, localized or extensive. Periosteal deposits were often present and in some cases the rarefactions extended into these or involved the medullary tissues. On resolution the periosteal deposits were usually absorbed or became organized on to the cortex before the cortical rarefactions were filled in. Although in a few cases no gross alterations in the bone resulted, often some thickening and expansion remained.

Tertiary bone lesions were more destructive and lasted longer than secondary bone lesions. They often ulcerated through the skin. The skull, ribs, clavicles and epiphyses were affected. A few instances of involvement of joints and of spontaneous fractures, especially of the phalanges, were observed. The vertebral column was not radiographed and no clinical evidence of its involvement was found at any stage. In the hands and feet, one or only few bones were affected and bones of the carpus and tarsus were involved in the tertiary stage.

The bone changes associated with tertiary yaws skin lesions, or with chronic non-specific skin ulceration consisted of periosteal deposits and cortical thickening and never of rarefied foci of any form.

A comparison of bone lesions of syphilis with those of yaws shows the great similarity between them. The periosteal deposits and cancellous tissue rarefactions of secondary yaws resemble changes of congenital and secondary acquired syphilis. Rarefactions in the cortex and in periosteal deposits in secondary yaws appear to be more marked and frequent than in congenital or acquired secondary syphilis. The periosteal deposits and cortical rarefactions of tertiary yaws closely resemble the gummatous lesions of late congenital syphilis and tertiary acquired syphilis. The bones affected in both diseases are similar. Joint lesions appear more frequent in syphilis. The absence in yaws of osteo-chondritis, so characteristic of congenital syphilis, may be due to the greater age of even the youngest yaws patient (over one year), while the greater frequency of dactylitis in yaws is a quantitative rather than a qualitative difference.

None of the points differentiating yaws and syphilitic bone lesions in published papers is applicable in general to yaws ; previously reported differences seem to be based on a small number of cases, and were found to be non-existent over the larger number and greater variety of cases forming the basis of the present study. In short, apart from the absence of osteo-chondritis in yaws, there is probably no bone lesion that occurs in one disease that may not be observed in the other. There is, however, need for a thorough investigation of the bone lesions of syphilis in Africans.

(Copies of this Thesis have been deposited in the Library of the London School of Hygiene and Tropical Medicine, the Library of the University of London, the Army Medical Library, Washington, and the Library of the School of Public Health and Tropical Medicine, Sydney.) *F. Murgatroyd*

LEPROSY

BISHOP, F. W., SUHRLAND, L. G. & CARPENTER, C. M. **A Comparative Study by Electron Microscopy of the Morphology of *Mycobacterium leprae* and Cultivable Species of Mycobacteria.** *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 361-6, 20 figs. on 5 pls.

This is an important paper illustrating varying appearances of acid-fast bacilli greatly magnified under the electron microscope. The bacilli are freed

from tissue by repeated centrifuging and by taking a loopful from the top layer of the sediment, which contains most of them. Both the bacilli of human and rat leprosy were examined, together with cultivable acid-fast bacilli, e.g., *Myco. tuberculosis*, *Myco. smegmatis* and *Myco. phlei* and the vole bacillus, and noteworthy differences between them are shown in illustrations of about 20,000 x magnification, which should be studied by those interested. The morphological pattern of *Myco. leprae* and *Myco. leprae murium* is much the same, and they differ from the cultivable mycobacteria in their internal structure. Polar bodies of increased density are present in all the bacilli examined. Bodies of type A are large and opaque with no definite signs of internal arrangement, and they have been identified as nuclei of the cells; bipolar orientation is common. They were found in the bacilli of tubercle, leprosy and rat leprosy. Bodies of the B type are small and thin, generally more numerous and not so prominent as the A type. Care is necessary to exclude artefacts. Changes in morphology may be induced by exposure *in vitro* to saponified fractions of moogrol, to oleic acid, by boiling in 0·85 per cent. saline and by strong bases or formaldehyde. This report is a preliminary one and further work on these lines will be awaited with interest. [Examination by the electron microscope of the acid-fast bacilli found by Moiser in cockroaches may well throw light on their real nature.] *L. Rogers*

MANALANG, C. **The Transmission of Leprosy.** Reprinted from *Monthly Bull. Bureau of Health.* Manila. 1948, July–Aug., v. 24, No. 4, 9 pp.

FLOCH, H. & CAMAIN, R. Aspects histopathologiques de la lèpre en Guyane française. [**Histopathological Features of Leprosy in French Guiana.**] *Bull. Acad. Nat. Méd.* 1948, v. 132, Nos. 35/36, 601–5.

The South American classification of leprosy of 1946 is based on histological changes, which are described in this paper as the result of 380 observations in 257 cases under treatment by the sulphones promin and diasone, in sections stained by haematin-eosin and by Ziehl's stain for bacteria. Lepra bacilli were found in 98 per cent. of lepromatous cases, in 80 per cent. of major tuberculoid, 22 per cent. of minor tuberculoid and in 33 per cent. of "indifferent" ones. Histological changes have confirmed in general the clinical diagnosis. Friction of cutaneous macules with caustic preparations produces infiltration with lymphocytes, histiocytes and fibrocytes and transforms anaesthetic into erythematous macules and leaves hyperpigmentation after several months. Histological examinations furnish more precise diagnostic indications than clinical ones. Moreover, histology reveals the persistence of tuberculoid changes after macules have lost their clinical tuberculoid appearance. The evolution of lesions under sulphone treatment can also be followed by means of histological examinations. The changes after treatment for a year corresponded with those described by FITE & GEMAR [this *Bulletin*, 1946, v. 43, 751]. These include a decrease in the vacuolated cells and an increase of lymphocytes and replacement of the leprous tissues by connective tissue and decrease of the infiltration of the tissues. These modifications are most rapid and marked in recent lepromatous lesions. On the other hand, the histological appearances of tuberculoid and indifferent lesions scarcely seem to be influenced by sulphone treatment. Histological examinations of sections for lepra bacilli are also more effective, although not so quick, as in broken-up tissues, for lepra bacilli are found more frequently in sections if three or four specimens are examined, especially in tuberculoid cases. The morphological changes in the bacilli can also be better observed in sections. Those situated near blood vessels are much more affected by sulphones in lepromatous lesions. On the other hand, the

bacilli of "indifferent" cases and in nerve trunks at a distance from blood vessels are little affected by sulphones; this explains the relatively slight action of sulphones in the last two types of leprous lesions as compared with lepromatous ones. *L. Rogers*

LEON BLANCO, F. & FITE, G. L. **The Effect of Fixatives on Staining Procedures for Lepra Bacilli in Tissues.** *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 367–8, 1 pl.

"For the demonstration of lepra bacilli in paraffin sections the following are recommended:—(a) Fixation in Zenker's fluid; (b) use of thin blocks, with minimal time in dehydrating and clearing fluids; (c) staining by the oil-fuchsin method, and (d) mounting in one of the modern synthetic mediums, 'clarite' or 'permount', never in balsam."

ARNOLD, H. L., Jr. **The Intradermal Mecholyl Test for Anidrosis; a Diagnostic Aid in Leprosy.** *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 335–46, 3 figs. on pl. [19 refs.]

The action of mecholyl chloride (stated to be pharmacologically "virtually identical with acetylcholine") as a test for loss of sweating power in leprosy in place of pilocarpine is described in this paper. After a brief description of the physiology of sweating, earlier reports on the use of mecholyl are summarized and the conclusion is arrived at that denervation of sweat glands by leprous neuritis is the cause of anidrosis usually affecting the most distal portions of the post-ganglionic nerve fibres. In carrying out the test, equal areas of leprous and adjoining healthy skin are painted with Minor's solution, consisting of crystalline iodine 2 grammes, castor oil 10 cc. made up to 100 cc. with absolute alcohol, which dries rapidly. Then 0·05 to 0·1 cc. 1 per cent. aqueous solution of mecholyl chloride is injected intradermally at the border of the lesion to produce a weal partly inside and partly outside the lesion: the whole area is quickly and lightly dusted with powdered starch from an atomizer. Within a few seconds sweat droplets appear on the functionally intact skin, which becomes black due to the iodine and starch combination. The response is negative when no sweat drops appear within the area tested. Quite exceptionally the reaction is doubtful if no more than 6 to 8 pinpoint-sized droplets can be seen on the area tested. In facial lesions it is doubtful if this test can be relied on as in the oval, hypopigmented, facial macules of achromia parasitica a sweat response is liable to be absent and not one of a series of these cases has developed leprosy. Macular or tuberculoid annular lesions showed the area of anhydrosis to correspond exactly with the area of involvement and demonstrable anaesthesia and the reaction is clear cut and evident even in dark-skinned patients. *L. Rogers*

VILANOVA, X. & ESTELLER, J. La radiografia de los nervios cubitales en los enfermos de lepra. [**Radiography of the Ulnar Nerves in Leprosy Patients.**] *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 351–60, 10 figs. on 4 pls. English summary.

The English summary of this paper states that the authors first give a brief review of the subject and then give their personal experience with this method of examination in support of the existence of the fibrous reactive leprosy of their classification. After proving the safety of their technique and the selection of thorotrast as the contrast substance, they carried out experiments in the cadaver. The ulnar nerve should be exposed surgically and thorotrast injected

in an upward direction with some pressure in amounts of 1·5 to 3 cc., and they report on 8 cases of fibrous reactive leprosy and 3 of tuberculoid reactive leprosy. The X-ray pictures are difficult to interpret and they only draw final conclusions regarding the fibrous reactive cases, namely that : " in classifying leprosy histologically the fibrous substratum has so dominant a role that in many of the patients there is not the slightest suspicion of a previous tuberculoid or lepromatous stage." *L. Rogers*

DHARMENDRA & MUKERJEE, N. **The Treatment of Leprosy with Hydnocarpus Remedies.** *Leprosy in India.* 1947, Apr., v. 19, No. 2, 36–43, 6 figs. on 4 pls.

FLOCH, H. & CAMAIN, R. Traitement de la lèpre par les sulfones (promin et diasone) en Guyane française. [**Treatment of Leprosy by Sulphones in French Guiana.**] *Bull. Acad, Nat. Méd.* 1948, v. 132, Nos. 35/36, 606-10.

This is a report on a trial of promin or of diasone in 52 cases for eight up to twenty months with favourable results in pre-lepromatous or lepromatous cases of a very similar nature to those already reported by others, but also dealing with indifferent and tuberculoid cases. Promin was given in daily doses gradually increased from 1 gramme to 2½ gramme and 5 gramme doses. Improvement of different degrees was observed in all, but was most marked in young subjects. Nine cases of the indifferent type were treated in young subjects, with improvement in six, no change in one and aggravation of the symptoms in two. The greatest benefit was seen in two pre-lepromatous cases. Of three tuberculoid cases in young subjects two remained stationary and one was worse. Cases which improved also showed favourable histological changes. Diasone was used in the usual doses in nine lepromatous cases with improvement in all of a similar nature to those obtained with promin. Of twelve indifferent cases in young people five improved and seven remained stationary. Of three reactionary tuberculoid cases and seven tuberculoid minor ones, nearly all in young persons, the first three lost their reactionary character, as often occurs without treatment. Of the remaining seven two were better, two unchanged and three were worse. The histological changes were similar to those after promin and reactions were not observed. Any anaemia was easily arrested by iron treatment. The lepra bacilli became granular, broke up and eventually disappeared in favourable cases and especially in the more vascular lesions. Neural cases with few bacilli were least favourably influenced by sulphone treatment. *L. Rogers*

SLOAN, N. R. **Effects of Sulfone Treatment on the Larynx in Leprosy.** *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 329–33.

The author records further evidence in support of his earlier experience of the favourable effects of sulphones in leprosy laryngitis in Hawaii. During less than two years up to the middle of March, 1948, 116 patients were treated with promin, and 114 with diasone and 15 with promizole. Of 197 patients never subjected to tracheotomy, 45 lepromatous ones had the cardinal symptoms of hoarseness or dyspnoea or both, but 37 of them (82 per cent.) improved apparently as the result of treatment and the remaining 8 only complained of hoarseness after short treatment. Of the improved cases at least two were saved from tracheotomy. A striking fact is that only one patient early in his treatment required this operation against 7 to 17 every year before sulphones were used. Moreover 9 patients have been able to remove their tubes, presumably as the result of sulphone treatment. Of 30 other patients, marked improvement in breathing and voice were noted in 19. Choking spells have

also been greatly relieved and chronic bronchitis due to tracheal tubes has disappeared. When a patient can inhale deeply with a finger over his tube and with little or no retraction of the suprasternal notch, and the cords, if they are visible, which may not be the case, move freely the opening of the tube is covered with adhesive tape : if the patient is able to breathe naturally for some days the tube may be removed and a dressing applied, under which healing may take place unless the sinus is lined with epithelium, when an operation may be necessary to close the opening. The author concludes that improvement in laryngeal lesions is perhaps the most striking result of sulphone treatment in leprosy. *L. Rogers*

FERNANDEZ, J. M. M., CARBONI, E. A., TOMMASINO, P. & GIMENEZ, M. M. **Hematologic Study of Leprosy Patients treated with Diasone.** *Internat. J. Leprosy.* 1948, July–Sept., v. 16, No. 3, 319–27, 2 figs.

This is a careful study of the blood changes that follow the use of diasone in Leprosy. Anaemia and depression were noted in 89 per cent. of cases, and most marked when the daily dose exceeded one gramme. They may appear during the first few weeks of treatment and subside on withdrawal of the drug. The red cells only exceptionally decrease by more than two million and the haemaglobin to under 50 per cent. ; even the worst cases respond favourably to withdrawal of the drug and the use of iron, liver and vitamin B complex. Severe leucopenia was not met with and there was an increase of reticulocytes proportional to the severity of the anaemia ; this indicates that the bone marrow is unharmed and the anaemia of the regenerative type. Urobilin—but not bile pigment—is found in the urine and red-cell resistance is decreased ; these indicate a toxic haemolytic effect. Indirect bilirubin determination was almost always negative. The anaemia is thus benign and rarely requires interruption of the treatment, especially if the daily dosage is restricted to one gramme daily. *L. Rogers*

DE SOUZA-ARAUJO, H. C. **Antileprosy Institutions in Brazil. Present Situation of the Federal, State and Private Organizations.** *Internat. J. Leprosy.* 1948, Aug.–Sept., v. 16, No. 3, 369–80.

CHIYUTO, S. **Reorientation of the Control of Leprosy with Emphasis on Infantile Susceptibility.** Reprinted from *Monthly Bull. Bureau of Health.* Manila. 1948, July–Aug., v. 24, No. 4, 10 pp. [16 refs.]

CHIYUTO, S. **Leprosy Control based on Transmission, Susceptibility and Pathogenesis.** Reprinted from *Monthly Bull. Bureau of Health.* Manila. 1948, July–Aug., v. 24, No. 4, 15 pp. [26 refs.]

HELMINTHIASIS

CALDERON RODRIGUEZ, Judith. Algunos datos sobre anthelminticos intestinales. [**Observations on Intestinal Anthelmintics.**] *Medicina.* Mexico. 1948, Dec. 10, v. 28, No. 569, 507–18. [Numerous refs.]

A survey and review of the literature.

DA SILVA, J. R. Novos aspectos da terapêutica da esquistossomiase mansoni. [**New Aspects in the Treatment of Schistosomiasis mansoni.**] Reprinted from *Vida Médica.* 1948, Dec., v. 15, No. 4, 13 pp. [42 refs.]

It is not easy to see in what respects these " aspects " are new. The author sketches the results which various investigators of repute have reported from the use of emetine hydrochloride, tartar emetic and fouadin in infestation by

Sch. mansoni and enters a further plea for proof of results by examination of ova obtained by rectal biopsy—a method to be preferred to faecal examination. [See this *Bulletin*, 1949, v. 46, 377.] *H. Harold Scott*

KIKUTH, W. & GÖNNERT, R. **Experimental Studies on the Therapy of Schistosomiasis.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 256–67.

Antimony compounds such as tartar emetic and fouadin and also emetine have been used in the treatment of schistosomiasis. The aim of the present therapeutic investigation was the discovery of a substance which could be given orally in the mass treatment of the infection. The researches were begun in 1932 and since *Schistosoma mansoni* develops to maturity in white mice it was employed chiefly in that host and in rhesus monkeys throughout these studies.

The vector snail was *Planorbis guadaloupensis* [*Australorbis glabratus*] and was maintained in small tanks with filtered water and sandy bottom in which various water plants were grown at a temperature of 26 to 28°C. The snails were fed on lettuce, small crustaceans, liver and earthworms. Ultra-violet irradiation at first aided cultivation of the snails but was later dispensed with. In order to infect the latter, washed eggs of *S. mansoni* from infected faeces were illuminated in water at 40°C. Miracidia soon emerged and infected snails placed in the water, one for each 30 schistosome eggs. At 26 to 28°C. the development to the cercarial stage in the snails occupied 4 to 7 weeks. The cercariae generally emerged at midday under the influence of heat and light and could be counted in suspension after being killed with formalin. Instead of immersing the animal to be infected, cercariae from different snails (to ensure mixing of the sexes), were injected subcutaneously, 50 to 60 for a mouse and 200 to 300 for a monkey. Sexual maturity of the schistosomes was attained in mice in about 6 weeks, when 2 to 12 pairs were usually present. Eggs were regularly present in faeces after the 48th day and chemotherapeutic tests were then begun.

The drug was given by mouth on 6 successive days. When treatment was directed against immature worms, the drug was given on the 33rd day after infection. The excretion of eggs while the animal was alive, the presence of live worms, eggs and pigment in the liver as well as the condition of dead worms all served as criteria of the effectiveness of a drug. On testing a large number of drugs, the active xanthones and thioxanthones named Miracil A, B, C and D, etc., were discovered. Cure could in some cases be effected by a single dose and it should be noted that " stools do not become free from eggs until 14 days after the beginning of treatment, even when a cure has been produced." The action of miracils was more pronounced against sexually mature forms. The activity of these compounds varied in the mouse and monkey host. Because of the favourable results obtained in monkeys, Miracil D was suggested for trial in human patients, but clinical tests could not be carried out by the authors on account of the late war. Reports on the clinical use of the drug by BLAIR *et al.* and WATSON *et al.* have appeared [this *Bulletin*, 1948, v. 45, 526, 1018]. Details of the pharmacology of Miracil D are also recorded [*ibid.*, 798]. These substances cause considerable changes, especially in female worms. Intestine, gonads and yolk-cells are affected and egg-production is disturbed. Their particular action on sex-organs may explain why immature worms are less susceptible. *J. D. Fulton*

VOGEL, H. & MINNING, W. **The Action of Miracil in** *Schistosoma japonicum* **Infections in Laboratory Animals.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 268–70.

In the preceding abstract, KIKUTH & GÖNNERT report favourably on the action of certain Miracil compounds (xanthones and thioxanthones) against

Schistosoma mansoni infections of mice and monkeys. In the present investigation rabbits, golden hamsters and rhesus monkeys infected with *S. japonicum* by the authors' own method were used (*Acta. Trop.*, 1947, v. 4, 21, 97). When infection was established, as shown by the discharge of ova, drug treatment was given by stomach tube or subcutaneously. Six different Miracil compounds, including Miracil A, B, C and D were used in doses which had proved effective against *S. mansoni*. Results were judged by daily examination of faeces and later by autopsies when the worms were collected from blood vessels, chiefly mesenteric veins, and examined. Attention was also paid to the viability of ova from intestinal mucosa. After staining of the worms slight effects of the drugs were noted in sex organs, and some worms were possibly smaller than normal. They were, however, not destroyed nor was the discharge of ova interrupted. This finding was in contrast to the effectiveness of the same Miracils against *S. mansoni*.

J. D. Fulton

OLIVIER, L. **A Note on Schistosomiasis in Eastern Japan.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 867–75, 2 figs.

Five schistosomiasis endemic areas are known to exist in Japan. That extending along the Tone River to the north and east of Tokyo is an important rice-growing region. The presence of *Schistosoma japonicum* infestation was here first demonstrated in 1914 ; although it has since been found in various localities the endemic foci have not been clearly defined. The author records information collected from available reports and literature on the subject, and has been able to add to this by a limited investigation of part of the Tone area. A total of 11 children, between 8 and 14 years, of 97 in an elementary school at Koya were shown, on the basis of a single stool examination, to harbour *S. japonicum* ; one of 75 children at Ono school, some 3 kilometres distant, was found infected. Cercariae of *S. japonicum* were recovered from specimens of *Oncomelania nosophora* from limited areas in the wet grassy parts of this district. The author believes the disease could be eradicated from the Koya area, as the distribution of infected snails is limited ; infected areas can be avoided ; and those who have to enter them, to cut grass, could wear protective clothing. Local instruction of the population should produce satisfactory results.

A. R. D. Adams

See also p. 428, HSU, **Malaria in Southern and Western Szechuan with a Note on the Occurrence of** *Schistosomiasis japonicum*.

DESCHIENS, R. & PICK, F. Conservation de *Watsonius watsoni* (Conyngham, 1904), amphistome de l'homme et des primates dans des conditions extérieures à l'hôte. [**Preservation of** *Watsonius watsoni* **under Artificial Conditions.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 7/8, 490–94.

Mature amphistomes (*Watsonius watsoni*) were obtained from several baboons (*Papio sphynx*) after autopsy and placed in various media at temperatures of 37°C., 20°C., 3°C. and 0°C. with the object of finding a method of keeping the worms alive outside the host. The most successful medium, in which the worms remained alive for 18 days, consisted of a mixture of extract of beef liver jelly and 8 per cent. physiological saline at *p*H 7·6. The optimum temperature proved to be 37°C. The worms were also kept alive for 13 days in a simple liquid medium consisting of one part of horse serum and seven parts of Ringer's solution, at *p*H 7.6 These results are maintained to have practical value in facilitating certain biological studies and also investigations *in vitro* with anthelmintics.

J. J. C. Buckley

ESKOLA, O. **On Reticulocytosis in Anaemia Perniciosa Diphyllobothrica during Liver Treatment, with consideration of the various Types.** *Ann. Med. Intern. Fenniae.* 1948, v. 37, No. 2, 91–115. [31 refs.]

The author has studied the reticulocyte response in 19 cases of anaemia associated with *Diphyllobothrium* infection, during treatment. The worm was removed by a dose of 3·5 to 4·0 grammes of oleo-resin of aspidium (*Filix mas*) followed by Epsom salts. An injection of 5 ml. (or 4 ml.) of Campolon was given on three successive days and then 15 ml. of liver extract daily by mouth. After an initial complete blood count and sternal puncture, differential reticulocyte counts were made daily and the sternal punctures were repeated each day up to the crisis and at the conclusion of treatment.

The author recognizes five groups of reticulocytes :—(0) nucleated, (I) glomerulo form, (II) reticular, (III) imperfect reticular, (IV) maturing form with small reticular remnants only.

In six normal controls there was no change in the reticulocyte percentages during treatment : in the peripheral blood the reticulocytes ranged from 0·2 to 1·0 per cent. and the ratios were groups I+II : groups III+IV : : 1 : 6·7 to 1 : 11·5 (average 1 : 8·6) ; whereas in the bone marrow smears they ranged from 0·4 to 2·2 per cent. with the ratios of groups I and II : groups III and IV : : 1 : 1·1 to 1 : 4 (average 1 : 2·4).

In the infected cases, the reticulocyte percentage in the peripheral blood was from 0·3 to 2·8 (average 1·1), and in the bone marrow it was 1 to 4 times that in the peripheral blood. The average ratio of the reticulocyte groups I+II : III +IV was 1 : 10·9 (*cf.* normal 1 : 8·6) in the peripheral blood, and 1 : 3·6 (*cf.* normal 1 : 2·4) in the bone marrow ; that is, the maturer forms are more abundant as a result of the slow emission from the bone marrow.

During treatment the reticulocyte percentage in the peripheral blood reached its peak (reticulocyte crisis) in 3 to 8 days : in patients with less than 2·5 million red cells per cmm. initially, the maximum percentage was always over 8, the highest being 22. In the bone marrow the crisis occurred on the same day or the day before.

During treatment the younger reticulocytes began to increase at a greater rate than the older ones, so that there was a shift to the left in the reticulocyte picture. This was most striking in the severe cases, in which the ratio I+II : III+IV changed from 1 : 12·4 before treatment to 1 : 4·3 during treatment.

This shift reached its maximum point on the day of, or on the day before, the reticulocyte crisis. It was apparent in both the peripheral blood and the bone marrow. After removal of the worms alone, the reticulocyte crisis occurs a few days later. *L. E. Napier*

ESKOLA, O. **Bone Marrow Picture in Early Remission of Pernicious Tape-Worm Anemia.** *Ann. Med. Intern. Fenniae.* 1948, v. 37, No. 2, 116–42. [40 refs.]

A series of 6 normal controls and 19 cases of *Diphyllobothrium* anaemia were studied before and after treatment.

In the 6 normal controls, the sternal marrow counts were similar to those given by other investigators with minor but not constant variations, and no material change was observed after liver administration. The erythroblastic series were from 20 per cent. to 29 per cent. of the total nucleated count and of these about 70 per cent. were normoblasts, most of the rest being macroblasts ; there were no megaloblasts.

In 12 cases of anaemia the worms were first removed by the administration of oleo-resin of aspidium (*Filix mas*) and Epsom salts before liver extract

(Campolon 5 ml. by injection followed by 15 ml. by mouth twice daily) was given, and in 7 the liver extract was given first, the worms not being removed.

In the untreated cases with severe anaemia—less than 1·5 million erythrocytes—the total erythroblast counts were from 41 per cent. to 64 per cent., of which from nil to 17 per cent. were normoblasts, 23 to 40 per cent. were proerythroblasts, and 19 to 33 per cent. megaloblasts. After liver administration, the total erythroblast percentage rose further and the proerythroblasts and megaloblasts disappeared within a day or two; at the end of a week a few macroblasts only remained, over 95 per cent. of the still high total red cell series being normoblasts; and after another month 100 per cent. were normoblasts, but meanwhile the total erythroblasts had fallen to 2 to 7 per cent. of the total nucleated cell count. In the less severe cases, the changes were less pronounced but materially the same.

In the severe cases in which the worms were not removed, there was at first a reduction in proerythroblasts and megaloblasts, but later these returned to more or less their pre-treatment percentages: however, there was little change in the erythroblast/leucoblast ratio and no increase in peripheral blood red cell count.

Myeloblasts were found in the bone marrow of the cases of anaemia prior to the treatment, 14·7 to 33·8 per cent., with an average of 20·5 per cent.; with intensive liver treatment they disappeared on the second or the third day of treatment. In the worm-carrier cases which were given inadequate liver treatment, they decreased to 0·6 to 1·7 per cent. on the third or the fourth day of treatment, after which they increased again.

The leukopoietic bone-marrow picture prior to the treatment was nearly normal, with regard to the percentages, or it showed a slight shift to the left; as regards numbers, however, it was increased. During intensive liver treatment, it subsided to normal level and moved slightly to the right.

Three to 7 weeks after the commencement of abundant liver treatment, a comparatively strong lymphocytosis (22 to 48 per cent. of all nucleated cells) occurred.

L. E. Napier

McMenemey, W. H. & Vickers, A. A. **Cysticercosis. Discussion and Presentation of a Case.** *Brit. J. Radiol.* 1949, Feb., v. 22, No. 254, 84–7, 3 figs.

Gault, E. W. & Balasubrahmanyan, M. **A Case of Cerebral Cysticercosis.** *J. Path. & Bact.* 1948, July, v. 60, No. 3, 505–6, 3 figs. on pl.

"A rapidly fatal case of cerebral cysticercosis is reported. The patient, a Hindu girl aged 14, had symptoms suggestive of cerebral tumour. The adult worm was found in the small intestine. The cysts showed no evidence of calcification and the cysticerci were alive. An intense inflammatory reaction had developed around the cysts and was considered to be responsible for the symptoms."

Saint, C. F. M. **Hydatid Disease: some Features, Familiar and not so Familiar.** *Clin. Proc.* Cape Town. 1948, Oct., v. 7, No. 10, 315–38, 19 figs.

An account which would—possibly did—furnish a good clinical lecture on the subject of hydatid disease, excellently illustrated by photographs. The main interest lies in the account of cysts being found in unusual situations, such as the erector spinae, the body of the kidney, the parotid, the neck tissues, the orbit and behind the eye.

H. Harold Scott

CENDAN ALFONZO, J. E. Relaciones de la hidatidosis hepático con la litiasis biliar. Litiasis hidática. Litiasis parahidática. Litiasis biliar común. [**Relation of Hydatid Infection to Biliary Lithiasis.**] *An. Facul. de Med. Montevideo.* 1948, v. 33, Nos. 8, 9 & 10, 879–956, 9 figs. [57 refs.]

PEREIRA, O. Observações sôbre a ação do hexylresorcinol e tetracloretileno nas infestações pelos ancilostomídeos, *Ascaris lumbricóides*, Tricocephalus trichiura e sua aplicabilidade no meio rural. [**On the Effects of Hexylresorcinol and Tetrachlorethylene in Ankylostomiasis, Ascariasis and Trichuriasis in Country Districts.**] *Rev. Serviço Especial de Saúde Publica.* Rio de Janeiro. 1948, July, v. 2, No. 1, 47–58, 2 charts. English summary (7 lines).

Measures to combat these helminthic infestations are largely educational and sanitary engineering, but treatment of patients is a necessary adjunct. It is with the latter that the author deals here. With these drugs he treated 607 schoolchildren between the ages of 7 and 16 in various educational establishments in Vitória, Espirito Santo, and 70 in Pedra Furada, a municipality of Minas Gerais. The 677 were divided into five groups: I. Receiving one treatment with hexylresorcinol—0·4 gm. for those under 6 years [but the ages are stated to be between 7 and 16], 0·6 gm. for those between 6 and 8 years, 0·8 gm. for the 9–12-year-olds, 1·0 mg. for those 13 years or over. II. Two treatments with hexylresorcinol, with an interval of 20 days. III. One treatment by tetrachlorethylene, 2 cc. in two doses one hour apart, and a saline purge one hour after the second cc. IV. Two treatments with tetrachlorethylene, with a 20-day interval. V. Treatment first by cristoids [hexylresorcinol ?] and then by tetrachlorethylene after an interval of 20 days.

The results of treatment were estimated by comparing the egg-content per gramme of faeces by the Stoll-Hausheer method before and after the treatment. For a more detailed study the patients were graded according to the degree of infestation. Those with ankylostomes were put into 4 groups: (1) with less than 500 ova per gm. of faeces; (2) those with 500–2,000 per gm.; (3) those with 2,000–5,000; and (4) those with more than 5,000.

For *Ascaris*: (1) Those with up to 20,000 ova per gm.; (2) those with 20,000–50,000; (3) those with 50,000–80,000; and (4) those with more than 80,000.

The use of the two drugs together reduced the figures by 94 per cent. for these two helminths; 98·5 per cent. of *Ascaris*, and 93·9 of ankylostomes. A single treatment by tetrachlorethylene alone was good in mild infestations by hookworms; it was useless in a little more than 60 per cent. of patients treated. Hexylresorcinol proved excellent for *Ascaris* infestation; with one course, 10 out of 38 with more than 80,000 ova per gm. were cured, with two courses 24 out of 25.

On *Trichuris* infestations the effects were poor, whether the drugs were used singly or in sequence and in one or two courses. Only 11·7 per cent. were returned as negative.

In conclusion, tetrachlorethylene has certain drawbacks to its use in rural districts, and the need for a saline purgative 3, 4, or more hours after the drug is taken "brings about such an outpouring of bile that the anthelminthic action is neutralized". Hexylresorcinol, however, is given once only and the patient can return to his normal activities; moreover, it is easier to take, as it is given in capsule form. The latter is, therefore, to be preferred for mass treatment in rural districts.

H. Harold Scott

MAO, C. P. **Occurrence of Dog Hookworm** (*Ancylostoma caninum*) **in Man.** *Chinese Med. J.* Chengtu Edition. 1945, Apr., v. 63A, No. 3, 130–32, 2 figs. [10 refs.]

Report of a case stated to be the second in the literature.

CATTAN, R. FRUMUSAN, P. & COUSIN, R. Syndrome de Loeffler symptomatique d'ascaridiose au décours d'un infarctus pulmonaire suppuré. [**Loeffler's Syndrome as Evidence of** *Ascaris* **Infection complicating a Septic Pulmonary Infarct.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1949, Nos. 1/2, 27–9.

A patient of 52 was undergoing treatment for an infarct of the left lung. Routine blood examination showed 7 per cent. eosinophiles which increased to 31 per cent. within the next month. An X-ray examination now showed a hazy infiltration of the *right* lung; this shadow had not been present at a previous routine X-ray examination (although evidence of the lesion in the left lung had) and it disappeared again within 2 weeks. During this time, the percentage of eosinophiles reached 39. A week later, the patient expelled 4 small *Ascaris* worms by the mouth, without effort. Despite this and the disappearance of the X-ray signs, the eosinophilia persisted at 24 per cent., accompanied by a total decrease of granulocytes (39 per cent.).

The special interest of this case lies in the fact that the time from the appearance of the fleeting infiltration in the right lung to the expulsion of the worms was only 20 days. Usually in such cases one has to wait two months or more before finding ova in the stools and hence incriminating *Ascaris* as the cause of the manifestations. *H. J. O'D. Burke-Gaffney*

ROGERS, W. P. & LAZARUS, Marian. **Glycolysis and Related Phosphorus Metabolism in Parasitic Nematodes.** *Parasitology.* 1949, Feb., v. 39, Nos. 3/4, 302–14, 6 figs. [40 refs.]

CHANCE, M. R. A. & DIRNHUBER, P. **The Water-Soluble Vitamins of Parasitic Worms.** *Parasitology.* 1949, Feb., v. 39, Nos. 3/4, 300–301.

ROGERS, W. P. & LAZARUS, Marian. **The Uptake of Radioactive Phosphorus from Host Tissues and Fluids by Nematode Parasites.** *Parasitology.* 1949, Feb., v. 39, Nos. 3/4, 245–50, 5 figs. [20 refs.]

TRIM, A. R. **The Kinetics of the Penetration of some Representative Anthelmintics and Related Compounds into** *Ascaris lumbricoides* **var.** *suis. Parasitology.* 1949, Feb., v. 39, Nos. 3/4, 281–90, 9 figs. [19 refs.]

CARTER, H. F. **Records of Filaria Infections in Mosquitoes in Ceylon.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 312–21, 1 map & 4 figs. on pl.

These records relate to filaria infections found in mosquitoes caught under natural conditions in Ceylon and the Maldive Islands; no experimental infections in laboratory-bred mosquitoes are included. The results obtained from different localities have been grouped in relation to the known endemicity of the human parasites—*W. malayi* and *W. bancrofti*, but it does not follow that all the infections recorded from endemic areas are necessarily of human origin; many may have been derived from domestic animals.

Three separate investigations were undertaken in the North-Western Province. In the first two investigations, mosquitoes were collected from the villages at least once each month, over a period of 3–4 days, by hand-catching in the mornings and by trapping in the evenings. In the third, they were collected during the night from cattle-baited traps only.

In the first series, 8,500 mosquitoes were dissected. Filaria infections were found in 31 from the endemic villages and in 11 from the others. The majority were caught in cattle-baited traps. In the second series of observations, 35,000 mosquitoes were collected. Approximately 32 per cent. of the total catch for both villages were obtained from houses, 10 per cent. from human-baited traps, and 58 from cattle-baited traps. The predominant mosquitoes were *Anopheles subpictus*, *Culex tritaeniorhynchus*, *Aëdes pallidostriatus*, *Mansonioides uniformis*, and *Aëdes pipersalatus*. In cattle-baited traps the most prevalent was *C. tritaeniorhynchus*. Infections with filaria larvae were found in 83 mosquitoes : 32 (in 8,325 dissected) from one village and 51 (8,932 dissected) from the other.

From May 1932 to March 1933, the village of Akaragama near Kurunegala was used as an entomological station and from observations made there is reason to believe that the great majority of filaria infections found in mosquitoes were not of human origin. Of 7,000 mosquitoes caught 24 species of culicines and 12 anophelines were represented. Approximately 2,500 mosquitoes were dissected and examined : 172 were found to harbour filarial larvae.

In the Eastern Province, Toppur, a Muslim village, is situated at the northern extremity of a large lake where *W. malayi* filariasis is severely endemic. In November 1932, of 1,944 mosquitoes collected over 70 per cent. were *Mansonioides*. Filarial larvae were found in 54 mosquitoes, all but one being species of *Mansonioides*.

In the Western Province, although cases of filariasis have been reported, the data available did not suggest that it was prevalent.

In the suburban areas of Colombo, of 2,500 blood films examined 130 have shown microfilariae. All were embryos of *W. bancrofti*.

In the houses, *Culex fatigans* was the dominant mosquito. Infections with filarial larvae were found in 87, giving an infection rate of 8·8. Of three infected mosquitoes, *M. uniformis*, caught in cattle-baited traps two harboured small developing forms in the thoracic muscles, and in another (*Armigeres obturbans*) three mature larvae were found in the proboscis.

These investigations showed clearly that filariasis due to *W. bancrofti* is widespread throughout the suburbs of Colombo and that the essential carrier is *Culex fatigans*.

The records for the Maldive Islands relative to the most southerly of the atolls were obtained during a brief visit made in the latter part of February and early March, 1943. Although microfilariae were found sparingly in the blood of 84 residents in the daytime, no night specimens could be collected. Of 196 female mosquitoes (159 *C. fatigans*) which were examined for filarial larvae, twelve (11 *C. fatigans* and one *C. sitiens*) were infected. In *C. fatigans* collected in the village of Hittadu the infection rate was 6·6, and in the island, where elephantiasis cases are segregated, it was 8.0 per cent. *P. Manson-Bahr*

Ehrich, W. E., Seifter, J., Alburn, H. E. & Begany, A. J. **Heparin and Heparinocytes in Elephantiasis Scroti.** *Proc. Soc. Exper. Biol. & Med.* 1949, Jan., v. 70, No. 1, 183–4, 2 figs. [15 refs.]

"Microscopic examination of a human scrotum amputated because of elephantiasis showed numerous heparinocytes around lymph and blood vessels. One hundred and twenty-six mg of purified heparin per kg of wet tissue was obtained. Based on the purified material, the scrotum contained at least 16,380 I.U. of activity per kg of fresh tissue. These findings are further evidence that mast cells are sources of heparin. They also explain the absence of thrombosis in elephantiasis."

KERSHAW, W. E., WILLIAMSON, J. & BERTRAM, D. S. **Chemoprophylaxis of Experimental Filariasis in the Cotton-Rat.** *Brit. Med. J.* 1949, Jan. 22, 130–32. [15 refs.]

The authors have shown [this *Bulletin*, 1949, v. 46, 69] that the results obtained in chemotherapeutic tests with wild cotton rats naturally infected with *L. carinii* must be interpreted with caution and after due consideration of the course of infection in untreated controls. They do not consider that infections produced in rats by colonies of mites (*Liponyssus bacoti*) maintained in a rat-nest and previously fed on the infected occupant are suitable for chemotherapeutic tests. In order to avoid unknown factors inherent in the above method of infection, they have exposed rats to controlled infection by about 20 mites per animal for approximately 24 hours, as previous work had shown that they were efficient vectors. In a group of 41 rats exposed to infection in this way, engorged mites were recovered from 37 of the rats and 35 of them (95 per cent.) later had microfilariae in their blood. Observation has shown [this *Bulletin*, 1948, v. 45, 265] that all worms are not transmitted from the mites in their first infected blood meal. To estimate the probable number transmitted to a rat, dissections of a series of the mites was made before, and of engorged mites after, the transmission meal.

This method of producing controlled infections has been employed in preliminary experiments on the prophylactic action of drugs. Since antrypol (Bayer 205, suramin), stilbamidine and MSb (a pentavalent antimony compound prepared by FRIEDHEIM *et al.*, whose constitution is *p*-melaminylphenyl stibonate [see this *Bulletin*, 1946, v. 43, 1124]) are known to be active prophylactic agents against trypanosome infections they were tested for similar properties against filarial infections in the cotton rat. Three groups of 10 rats were used and received single doses intraperitoneally of different amounts of the three drugs. They were then exposed to the bites of infected mites along with 10 untreated controls. The infections were allowed to run their natural course and examinations were made at intervals for microfilariae and adult worms. Protection was not afforded by antrypol or stilbamidine. Rats receiving MSb were examined at intervals over a period of 4 to 9 months after exposure to infection for the presence of adult worms, since no microfilariae were detected. It was found that a dose of 250 mgm. of the drug per kilo. of weight was an effective prophylactic for a period of three weeks after administration.

J. D. Fulton

BROOKS, T. J., Jr., WARD, J. W. & HOLDER, T. M. **Studies on the Incidence of Trichiniasis in Mississippi. Preliminary Report.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 863–6. [12 refs.]

" (1) Diaphragms obtained from fifty negro cadavers in the Department of Anatomy at the University of Mississippi School of Medicine have been examined by the digestion and compression techniques for the presence of the larvae of *Trichinella spiralis*.

" (2) Three of the fifty diaphragms examined, or 6 per cent., were found to harbor the parasite.

" (3) Difficulties encountered in establishing both clinical and post-mortem diagnoses are commented upon.

" (4) It is anticipated that this series will be enlarged as more specimens become available from time to time."

BROWN, M., CRONK, B., deSINNER, F., GREEN, J. E., GIBBONS, J. E. & KUITUNEN-EKBAUM, E. **A Note on Trichinosis in Animals of the Canadian Northwest Territories.** *Canadian J. Pub. Health.* 1949, Jan., v. 40, No. 1, 20–21.

OLIVER-GONZÁLEZ, J. & BUEDING, E. **Reduction in the Number of Adult *Trichinella spiralis* in Rats after Treatment with Naphthoquinones.** *Proc. Soc. Exper. Biol. & Med.* 1948, Dec., v. 69, No. 3, 569–71.

"The oral administration of 2-methyl-1, 4-naphthoquinone and 2-hydroxy-3-piperidinomethyl-1, 4-naphthoquinone to rats infected with *Trichinella spiralis* produced a significant reduction in the number of intestinal adult trichinellae. Nine other structurally related naphthoquinones had no such effect."

DEFICIENCY DISEASES

YI, Chien-lung, CHAO, H., CHOW, Yen-chiao & LIU, Yun-moy. **Total Serum Protein Level in Normal Adult Chinese.** *Chinese Med. J.* 1948, Sept., v. 66, No. 9, 477–82. [24 refs.]

"1. The total serum protein concentrations of 1,954 normal adult male and 109 normal adult female Chinese were studied.

"2. It was found that the total serum protein level is within the normal range in merchants, medical personnel and most of the college students, but there was a slight hypoproteinemia in the majority of the soldiers, policemen, the servants in institutions and civil government employees.

"3. The serum protein level was found to vary with the quality of the diet. A diet containing more proteins seemed to increase the total serum protein concentration."

HAEMATOLOGY

DACIE, J. V. & WHITE, J. C. **Erythropoiesis with particular reference to its Study by Biopsy of Human Bone Marrow : a Review.** *J. Clin. Path.* 1949, Feb., v. 2, No. 1, 1–32, 58 figs. (34 coloured) on 5 pls. & 5 text figs. [Numerous refs.]

BIGGS, Rosemary & MACMILLAN, R. L. **The Errors of some Haematological Methods as they are used in a Routine Laboratory.** *J. Clin. Path.* 1948, Nov., v. 1, No. 5, 269–87, 14 figs. [30 refs.]

It has been usual for the standard of precision of a method to be based on the observations of a single expert in the particular technique ; in the circumstances the error that is exhibited has often little relation to the error that might be expected from the laboratory worker of ordinary skill doing routine examinations. The authors have endeavoured to estimate the error of the method and range of "normal" readings that may be expected from a working laboratory, in carrying out the following procedures :—the red cell count, the packed cell volume, the reticulocyte percentage, the haemoglobin percentage, the Price-Jones curve, the platelet count, the red cell fragility, and the whole blood coagulation time.

The results have been treated statistically and are shown in numerous tables. Some of the ranges ($\pm 2 \times$ standard deviation) are shown below :—

Haemoglobin	87–107% (Haldane) 91–103% (neutral grey).
Red cell count	3·56–5·22 millions.
Haematocrit	44·7–46·3 (Wintrobe).

Mean cell diameter ...	6·58–7·50 μ (100 or 500 cells measured on one slide). 6·86–7·22 μ (500 cells on 5 slides by 5 observers).
Reticulocyte percentage...	1·2–10·8% (dry) 1·0–13·4% (coverslip).
Platelets	63–667 thousands (Dameshek) 134–358 (Lempert).
Coagulation time ...	4·35–5·25 min. (Lee & White) 1·04–1·96 (Dale & Laidlow).

The ranges of some of the calculated indices are :—

Colour Index	0·87–1·36 (Haldane) & 0·90–1·34 (neutral grey).
M.C.H.C.	28·26–34·62 & 29·5–33·4%.
M.C.V.	84·4–124·8 cu. μ.

The authors remark in the discussion that " It may well be thought that the large errors obtained, in most cases larger than any previously recorded, are proof that none but those highly skilled can carry out these investigations adequately. To some extent this is true, for many of the techniques can be used with far greater precision. The Haldane method for haemoglobin estimation, for example, a notoriously unreliable method in routine practice, can give very uniform results in the hands of one observer." And in the summary they note that " In the diagnosis of anaemia the most precise measurements found in this investigation were : haemoglobin determination using oxyhaemoglobin and a neutral grey photometer, the haematocrit, the mean corpuscular haemoglobin concentration, and the mean cell diameter derived from the Price-Jones curve.

" The red cell count has an error of 9 per cent. and thus the colour index and mean corpuscular volume are too variable to record the small differences of interest to the clinician. The routine use of these indices might be restricted to the study of macrocytic anaemia in laboratories where a Price-Jones apparatus is not available." *L. E. Napier*

BIGGS, Rosemary & MACMILLAN, R. L. **The Error of the Red Cell Count.** *J. Clin. Path.* 1948, Nov., v. 1, No. 5, 288–91. [11 refs.]

Experiments were designed to find the origin of an irreconcilable discrepancy between the opinions of two groups of workers on the degree of difference allowable between the counts made in different squares of the haemocytometer. Wintrobe and others claim that, if the counts differ by more than 18 cells, it is an indication that the mixing of the red cells was imperfect, and they consider that such counts should be discarded. Other workers have claimed that a greater difference between counts in different squares is inevitable, since the red cells in a haemocytometer are subject to the Poisson distribution and that a difference up to 40 cells is possible without necessarily indicating an error of technique.

The experiments showed that there was on the part of technicians a bias in favour of uniformity in replicate counts ; this false uniformity did not tend to increase but rather to decrease accuracy.

The authors concluded that (1) in training workers to make routine red cell counts, they should not be encouraged to achieve agreement between replicate counts, but to make accurate counts ; (2) in making a red cell count a difference up to 40 cells should be allowable between the counts in the five separate squares counted ; and (3) the standard error of red-cell counts lies between 8 and 10 per cent. *L. E. Napier*

ROBERTS, J. I. **Normal Haematological Standards for Nairobi, Kenya.** *J. Trop. Med. & Hyg.* 1948, Dec., v. 51, No. 12, 254–9.

Total blood counts were performed on 200 healthy male European adults, drawn from military units, who had been resident in Nairobi, Kenya Colony, for at least three months. The ages of these men ranged between 20 and 30 years. Nairobi lies practically on the Equator at an altitude of about 5,500 feet. The climate is temperate, the humidity is low, the rainfall being on an average 32 inches per annum and there is a daily range of temperature as much as 30° to 40°F.

The haemoglobin was estimated with a Hellige acid-haematin haemometer (17 gm. of oxyhaemoglobin in 100 cc.=100 per cent. haemoglobin). The average value for these men was 20·06 gm. per cent. The average red cell count was 6,039,000 per cmm., and the white cells were 7,600 (49 per cent. polymorphs, 42 per cent. lymphocytes). A small group of men were studied from their arrival at Mombasa, on the coast, until a month after residence in Nairobi. There was only a very slight rise in the red cell and haemoglobin values during this period. In other words, the effects of altitude are not felt for a month or longer. The well-marked absolute and relative increase in lymphocytes has been noted before at high altitudes and in the tropics generally, and is thought to be due to the greater amount of ultra-violet radiation.

The author truly states that much remains to be done in the investigation of life at high altitudes; it is still quite uncertain how far (*a*) altitude, and (*b*) the sun's rays at the Equator affect the general physiology of man, including his mental state. *P. C. C. Garnham*

See also p. 432, ROBERTS, **A Comparison of Haematological Results in Europeans and Africans suffering from Active Malaria.**

PASSMORE, R. **Severe Anaemia in Indian Sepoys (Refractory Tropical Macrocytic Anaemia).** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan., v. 42, No. 4, 367–80. [12 refs.]

"An account is given of 127 cases of severe anaemia with haemoglobin levels below 4·0 grammes occurring amongst Indian sepoys evacuated from the Burma campaign.

"The majority had had recent malarial infections, and just under half presented evidence of a defective nutrition. Ancylostomiasis was not frequent.

"A variety of haematological types occurred, but the majority were macrocytic anaemias.

"Many of the patients differed from cases of tropical macrocytic anaemia as usually described in that they were refractory and did not respond to either yeast or parental liver therapy. Repeated blood transfusions were found to be the most important therapeutic agent."

There were 48 deaths (38 per cent.) in the series.

[The paper is mainly of value from a negative point of view; that is to say the author has shown that the anaemias encountered did not fall into any recognized groups, were of uncertain aetiology, and did not respond to recognized forms of treatment. He concludes with a suggestion that is little more than a guess and is certainly not a legitimate deduction from the data presented. It is, however, quoted below because the reviewer believes there is much truth in it.]

"Both the clinical and epidemiological evidence would suggest that we must look back into the past, before the beginning of the war, for the ultimate origin of these anaemias. It is probable that certain sepoys entered the Burma

campaign with a defence mechanism less well equipped than normal to withstand the haematological strains imposed by a period of defective rations and a simultaneous malarial infection. In the great majority of both British and Indian men at risk the bone marrow reacted vigorously and, as soon as the extra strain was removed, the blood was returned to normal. In this small minority the marrow appeared unable to react adequately and a long period ensued of impaired function often terminating in physiological failure sometimes with complete aplasia. This inadequacy of the bone marrow might be the result of repeated previous strains in childhood and youth, probably either from long standing nutritional defects or repeated malarial infections." *L. E. Napier*

SINGER, K., ROBIN, S., KING, J. C. & JEFFERSON, R. N. **The Life Span of the Sickle Cell and the Pathogenesis of Sickle Cell Anemia.** *J. Lab. & Clin. Med.* 1948, Aug., v. 33, No. 8, 975–84, 3 figs. [23 refs.]

In a study of the pathogenesis of sickle-cell anaemia, the authors carried out cross transfers of red cells between healthy persons with the sickling trait and patients with sickle-cell anaemia. The fate of the transferred cells was followed by agglutination tests ; their identity was ensured by transferring O cells to AB recipients or cells containing the N agglutinogen to M or MN recipients. The survival times are shown in graphs.

The cells from healthy persons with the sickling trait when transferred into patients with sickle-cell anaemia had disappeared at the end of an average period of 120 days (the generally accepted normal life span of the red cell) ; graphs showing the percentage survival during the period are linear.

When cells from a patient with sickle-cell anaemia were transferred to a healthy person with the sickling trait, the last surviving cells had disappeared after an average period of 34 days (actually 13, 30 & 58 days).

From this the authors conclude that the pathogenic principle operating in sickle-cell anaemia resides within the red cells themselves and that no extracorpuscular mechanism can be held responsible for the haemolytic syndrome.

They also conclude that :—

"Trait cells can be used safely for therapeutic transfusions.

"An analysis of the known facts about the sickling phenomenon shows that the sickling process which is the expression of an abnormality of the stroma does not lend itself to a satisfactory explanation of the pathogenesis of the anaemia. The hypothesis is formulated that sickle-cell anaemia develops because of an additional alteration in the cyto-skeleton which is qualitatively different from the structural anomaly responsible for the sickling phenomenon."

L. E. Napier

DALAND, Geneva A. & CASTLE, W. B. **A Simple and Rapid Method for demonstrating Sickling of the Red Blood Cells : the Use of Reducing Agents.** *J. Lab. & Clin. Med.* 1948, Sept., v. 33, No. 9, 1082–8. [15 refs.]

The phenomenon of sickling is dependent upon the concentration of reduced haemoglobin in the blood, and appears when the tension of oxygen in the gas phase with which the blood is in equilibrium is below 40 to 45 mm. of mercury. Practically all methods of demonstrating the presence of the sickling phenomenon depend on the production of reduced haemoglobin, by reducing the oxygen directly by exhaustion or replacement or by excluding oxygen while the haemoglobin is reduced by metabolic processes.

The authors have devised a simple method by which the haemoglobin is reduced by a chemical agent.

"A drop of a five-fold aqueous dilution of Cevalin (approximating a 2 per cent solution of buffered ascorbic acid, also containing 0·11 per cent sodium bisulphite), or a drop of 2 per cent sodium bisulphite, $Na_2S_2O_5$, is added to a small drop of the patient's blood on a glass microscope slide. After mixing, a cover slip is dropped on the preparation and excess blood is expressed by gentle pressure in order to produce a film of blood sufficiently thin to permit inspection of individual red cells under the high-power dry objective of the microscope. With the diluted Cevalin solution, sickling of the blood usually appeared within an hour, and with the 2 per cent. bisulphite solution it was often present within fifteen minutes at room temperature."

In 80 experiments, sickling was observed within 15 minutes in 9 instances, within one hour in 60, within two hours in 77, and within 3½ hours in every instance, when the ascorbic acid solution was used.

The authors also note that formalin, but not by virtue of its reducing properties, fixes the blood in whichever stage it comes in contact with it, that is either sickled or unsickled. Zenker's fluid, however, causes a reversal to the discoid forms when it comes in contact with sickled blood. This fact is of importance when treating tissues with these fluids: the former should always be used where sickling is to be demonstrated histologically. *L. E. Napier*

VENOMS AND ANTIVENENES

GOYAL, R. K. **Standardization of Daboia and Cobra Antivenines.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan., v. 42, No. 4, 381–92.

"Widely divergent amounts of test venoms are neutralized by the same amounts of their corresponding antivenines, when the mixtures are injected into different animals by different routes or in the same animal by different routes.

"There is no definite proportion between the quantity of antivenine and the amount of venom neutralized at different levels of test.

"Different batches of cobra and daboia venoms differ appreciably in potency. It is therefore inadvisable to indicate the titre of an antivenine in terms of mg. of venom neutralized. It should be stated in terms of the number of CLDs neutralized.

"A suitable method of titration of cobra and daboia antivenines has been described."

SERGENT, Et. De l'utilisation du DDT contre les scorpions. [**DDT for dealing with Scorpions.**] *Arch. Inst. Pasteur d'Algérie.* 1948, Dec., v. 26, No. 4, 397–401.

The author has carried out two series of experiments, one with a 20 per cent. emulsion of DDT, the other with a powder containing 5 per cent. DDT.

I. *Trials with Neocidol Emulsion.*—A preliminary experiment [the purpose of which is not quite clear] was carried out in which 10 specimens of *Prionurus australis* (the most dangerous of the North-African scorpions) were plunged for 5 minutes in the emulsion of DDT, 10 others being submerged in tapwater for the same time. All the former died in 24 hours; all the latter survived. Next 8 were immersed for one second in the emulsion and 7 of them were dead in 3–4 days.

Trial was then made to find out whether transitory contact with the emulsion, as the passing through it to enter dwellings, would be effectual. The emulsion was sprayed on the bottom and sides of a bowl (*bocal*), and two days later

8 scorpions were placed in it ; one only died and that in 3 days. Hence, spraying of the ground and walls with such a suspension would afford no protection.

II. *Trials with Neocidol powder containing 5 per cent. DDT.*—Two cages similar in every respect were used and each had two cartons with folded edges to offer shelter for the scorpions and the floor was sanded. Thirty scorpions were placed in each cage ; those in one were sprinkled with the powder, the others served as controls. The former at first appeared excited, but in half an hour settled quietly. Then toxic symptoms were observed—tremors and convulsive movements, lowering of the tail, pincers open—and they died, one in 2 hours, 4 more during the first day, 8 on the second, and altogether 22 in the first 6 days ; the others lived longer, one for 41 days, but by then all were dead. Of the controls 3 had died in the 41 days, " the average loss among scorpions kept in captivity without food."

Lastly, 12 scorpions, 10 adults and 2 young ones, were placed in a similar cage, and the powder was dusted once only at the base of the sides and the " shelters " ; 13 others (10 adults, 3 young) were placed in a similar but undusted cage, as controls. The former showed no aversion to the DDT, though their ventral surfaces came in contact with the powder. Two were dead in 2 days and 9 in 9 days ; the others died on the 13th, 16th and 28th days.

The conclusion is that DDT can be used with success against *Prionurus australis* provided the drug is in the powder form. This scorpion is nocturnal in its movements into dwellings from without and it crawls up walls and along wooden surfaces, so the powder should be spread between its haunts and beds and bedrooms.

H. Harold Scott

DERMATOLOGY AND FUNGUS DISEASES

BRICEÑO ROSSI, A. L. Carate o mal del Pinto. [**Carate or Pinta.**] *Bol. Laboratorio Clinica " Luis Razetti ".* Caracas. 1948, Mar. & Nov., v. 15, Nos. 25/26 & 27/28, 255–77 ; 291–2. [Refs. in footnotes.]

The first and greater part of this contribution consists of a general description of *mal del pinto.* The paper was read at a medical congress in Mexico City in December, 1947. The important part from the point of view of readers of this *Bulletin* is that which discusses the differences between Venezuelan and Mexican pinta on the one hand and the Cuban form on the other. In the latter, aortitis is fairly frequent and palmar and plantar hyperkeratosis, and doubt arises as to how much of the Cuban pinta is really yaws, or bejel, or even just syphilis, and whether the Mexican (or Venezuelan) and the Cuban pintas are merely different types of the same disease. The question is left undecided.

H. Harold Scott

HAUSMAN, R. Over Mycetoma Pedis (Madura-Voet). [**A Case of Madura Foot.**] *Med. Maandblad.* Batavia. 1949, Jan. 1, v. 2, No. 1, 5–8, 4 figs. on pl.

The English summary appended to the paper is as follows :—

" Description of a case of mycetoma pedis (Madura-foot) from the island of Lombok."

SALVIN, S. B. & HOTTLE, G. A. **Factors influencing Histoplasmin Formation.** *J. Bacteriology.* 1948, Nov., v. 56, No. 5, 541–6, 1 fig. [11 refs.]

By means of a complement-fixation test (which preliminary studies showed to be more satisfactory than the usual skin test) the conditions influencing histoplasmin formation by *Histoplasma capsulatum* were investigated.

In a medium consisting of *l*-asparagine, 14 gm. ; glucose, 10 gm. ; glycerol, 25 gm. ; magnesium sulphate ($MgSO_4.7H_2O$), 1·5 gm. ; dipotassium phosphate (K_2HPO_4) 1·31 gm. ; sodium citrate, 0·9 gm. ; ferric citrate, 0·3 gm. ; water to 1 litre, the maximum yield of histoplasmin was obtained after 8–10 weeks at room temperature. Replacement of the glucose by 10 gm. of cellobiose, dextrin, starch, or glycogen increased the production of histoplasmin from four to eight times. An initial *p*H of 7·0–8·0, a surface to volume ratio of near unity, and a temperature of 25°C. were found to be optimal for histoplasmin production while light, submerged or surface growth, and strain of the fungus were not critical factors. *G. C. Ainsworth*

Done

EMMONS, C. W. & ASHBURN, L. L. **Histoplasmosis in Wild Rats. Occurrence and Histopathology.** *Pub. Health Rep.* Wash. 1948, Oct. 29, v. 63, No. 44, 1416–22, 2 figs.

In a previous paper, EMMONS, BELL and OLSON [see this *Bulletin*, 1948, v. 45, 207] described the discovery of histoplasmosis in 10 wild rats and one mouse. The present report deals with the same group of animals, to which 6 more rats have been added. These 16 rats were among 565 trapped in Loudoun County, Virginia, in an area in which human and canine cases of histoplasmosis had occurred. In all cases the diagnosis of the infection in the rats was based on the isolation of *Histoplasma capsulatum* from the spleen and liver and less frequently from the lungs. Macroscopic lesions were seen in only four of the animals, but all of these were not attributable to histoplasmosis. Microscopically, the characteristic lesion of histoplasmosis was an " epithelioid " cell granuloma with a few microphages and fibroblasts and rarely a giant cell. These granulomata, which occurred chiefly in the spleen, liver, lung and adrenal, were sharply defined and measured from 30 to 200 μ in diameter. *H. capsulatum* was seen in sections from the lesions of nine of the animals. *J. T. Duncan*

SMITH, C. E., BEARD, R. R. & SAITO, Margaret T. **Pathogenesis of Coccidioidomycosis with special reference to Pulmonary Cavitation.** *Ann. Intern. Med.* 1948, Oct., v. 29, No. 4, 623–55, 5 figs. [44 refs.]

This is an important paper which should be read in the original.

In reviewing the pathological features of coccidioidomycosis, the authors state, in relation to the grave but relatively uncommon disseminated granulomatous form of the disease, that " Army experience also has indicated that dissemination usually occurs soon after the infection is acquired, frequently within a matter of weeks and infrequently after months ". This is in marked disagreement with the view expressed by FORBUS and BESTEBREURTJE (*Military Surgeon*, 1946, v. 99, 653), that disseminated coccidioidal granuloma is a reinfection phenomenon which may develop at any time up to about ten years after the original infection.

Pulmonary cavitation was found in from 2 per cent. to 8 per cent. of different series of cases of clinical coccidioidomycosis in the U.S. Army, and about 90 per cent. of the cavities were single. Cavitation may develop in pneumonic patches within the first few weeks of the illness, or up to some months after infection, and in more than half the cases it gave rise to no observed symptoms but was only discovered in the course of routine radiography. The cavities tend to close spontaneously and, in the early stages, complete rest until the general symptoms have subsided hastens the healing processes, but a cavity may sometimes persist and, if it causes symptoms, may require treatment by phrenic crush or even a more drastic surgical procedure. Cavitation is not caused by a progressive local coccidioidal lesion ; in fact, it is usually associated

with a demonstrable degree of acquired immunity and it may be accepted as a good prognostic sign for the authors say : " We have never seen dissemination occur in a patient with coccidioidal cavitation ". *J. T. Duncan*

RECTOR, L. E. & RECTOR, Eleanor J. **Coccidioidomycosis in the Salivary Gland of the Townsend Mole.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 707–9, 2 figs.

Two Townsend moles (*Scapanus townsendii*) were caught and killed in the Fauntleroy District of Seattle, Washington State, in 1934. The salivary glands were removed, fixed in 95 per cent. alcohol and examined for intranuclear or cytoplasmic inclusions. No inclusion bodies were found, but aggregations of fungal cells were seen in the parenchyma of the glands. These fungal cells were spherical and measured, on an average, 15·3 to 17·1 μ in diameter, the limits being 12·3 and 20·5 μ. Budding forms were not seen and there is no reference to endospores. [Two competent pathologists appear to have identified the fungus as *Coccidioides immitis*, but this diagnosis is difficult to reconcile with the authors' description of the parasite and the photomicrographs of the gland sections. It seems significant, also, that although 15 years have elapsed since this apparent discovery, no further record of coccidioidal infection in the north-western United States has appeared. Another fungal parasite of desert rodents, *Haplosporangium parvum*, which might be mistaken for *C. immitis*, has a much wider geographical distribution and has been found as far north as Alberta, Canada.] *J. T. Duncan*

MUENDE, I. **Treatment of Fungus Diseases of the Skin.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Nov., v. 42, No. 3, 216–22.

This paper should be read in the original by all who are interested in the control of ringworm infections.

Despite the great amount of research on the chemotherapy of the dermatophytoses and the very numerous fungicides available, it must be admitted that the drug treatment of some forms of tinea capitis and tinea pedis is frequently unsatisfactory. In the main, treatment tends to be based more on physical than on chemical methods ; thus epilation, avulsion of the nails and the use of keratolytic agents still play a major part in therapy. Dr. Muende gives timely warning against the use, in certain forms of athlete's foot, of irritant or excessively stimulating fungicides, even those of recent introduction, because of the danger of causing sensitization or chemical dermatitis. However, stimulating drugs such as chrysarobin and the much advertised phenyl mercuric compounds are valuable in the treatment of chronic and resistant infections. The propionates and undecylenates, from which much good was expected in cases requiring prolonged treatment, have proved rather disappointing.

On the important question of the need to use X-ray epilation in the treatment of tinea capitis, Dr. Muende points to the good results obtained by topical application of mild chrysarobin ointment followed by mechanical epilation of the loosened hairs when the infecting species is *Microsporon canis*, and he refers to the recent success claimed by Brain and others in the treatment of *Microsporon audouini* infection of the scalp by the application of phenyl mercuric nitrate in a carbowax base.

For established onychomycosis, avulsion of the nail plate combined with the application of fungicides to the nail bed is still the treatment of choice. The temporary avulsion, however, is frequently followed by recurrence of the disease in the new nail, and permanent avulsion of the finger nails is aesthetically

objectionable. Further research should be made on the use of fungicidal natural antibiotics, and another line of research recommended is on the use of fluorescent dyes which, when fixed by the fungus, render it highly susceptible to the action of ultraviolet rays ; but dyes which fluoresce to the more penetrating rays of the red end of the spectrum may be even more valuable.

For the prevention of tinea capitis, diagnosed cases should be isolated and treated and all contacts should be kept under observation, with repeated examinations, for 2 or 3 weeks to detect carriers and new infections. The control of the more widespread tinea pedis is impracticable except in the case of more or less closed communities. *J. T. Duncan*

HEAT STROKE AND ALLIED CONDITIONS

GALVÃO, P. E. **Human Heat Production in relation to Body Weight and Body Surface. I. Inapplicability of the Surface Law on Lean Men of the Tropical Zone.** *J. Applied Physiol.* 1948, Nov., v. 1, No. 5, 385–94, 2 figs. [11 refs.]

GALVÃO, P. E. **Human Heat Production in relation to Body Weight and Body Surface. II. Inapplicability of the Surface Law on Well Proportioned Men of the Tropical Zone.** *J. Applied Physiol.* 1948, Nov., v. 1, No. 5, 395–401, 2 figs.

CROWDEN, G. P. **A Survey of Physiological Studies of Mental and Physical Work in Hot and Humid Environments.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Jan., v. 42, No. 4, 325–35, 2 figs. [20 refs.] Discussion 336–40 [WEINER, J. S. ; MCROBERT, G. ; ALAKIJA, O. B. ; TIDY, H. ; WATTS, J. C.].

In this very interesting paper the author gives a review of physiological and psychological studies of the effects of work in hot places. Starting with the early observations of BLAGDEN and FORDYCE (1774) he attempts an appreciation of the work of various researchers. Much work on reactions to heat and humidity has been carried out with the purpose of helping men to face difficult climatic conditions in times of war, and the primary object of this paper is to interpret the knowledge so gained so that its use may contribute to human welfare in times of peace.

Much of the more recent work deals with the physiological or mental efficiency of carefully selected subjects, physically fit and young. Crowden very pertinently points out that these subjects were in an optimum condition of health, and had a maximum capacity to withstand fatigue, and that in attempting to apply the experimental result to the general population this very important fact must be borne in mind. He feels that the observations should be carried further to ascertain the reactions of a representative selection of a normal population.

After the presentation of the paper there was an interesting discussion. Sir George MCROBERT made biting comment on the way in which English officials in the tropics bedeck themselves with the habiliments of England and, worse, their attempts to induce indigenous inhabitants to follow suit. Dr. J. S. WEINER discussed the effects of air movement and radiant heat, the effects of acclimatization, and tropical anhydrosis.

Replying to the discussion, the author referred to the reduction in air movement within a mosquito net, and the consequent increase in effective temperature, and to the need for further studies of tropical clothing. *Thomas Bedford*

MISCELLANEOUS DISEASES

MACKAY, D. **Cancrum Oris among African Natives.** [Memoranda.] *Brit. Med. J.* 1949, Feb. 5, 223.

The prognosis of this condition has been regarded as almost hopeless. An infection with spirochaetes and fusiform bacilli is considered to be the probable cause.

The author did not see a single case while working in Great Britain in a highly industrialized area, but in the Serenje district of Northern Rhodesia he met with five cases in three years, three of these being fatal. Of the two patients who recovered, one was treated by extensive resection of the gangrenous area followed by plastic repair, the other with penicillin and this case is reported in detail.

A girl, aged about two years, was admitted to hospital on Oct. 3, 1947, clinical examination showing a typical early case of cancrum oris. The next day the brother of the above, aged four, was admitted moribund with the same disease, and died within 24 hours.

The girl was treated at first by swabbing with a strong solution of potassium permanganate, but the ulceration progressed. On Oct. 10, treatment with penicillin was begun, 10,000 units in aqueous solution being given intramuscularly every three hours. After the third injection, treatment was stopped for twelve hours owing to superstitious objections by the parents. Injections were then resumed and continued until 500,000 units had been given. Improvement was shown after 24 hours, and after three days all signs of infiltration of the surrounding tissues had disappeared and the ulcer showed a clean and healing surface. Recovery was uninterrupted and the patient was discharged on Oct. 27. It seems probable that the male child infected the female.

In none of the cases was there a previous history of specific illness and the author thinks that the chief cause is the poor diet and unhygienic life of the African. It may be noted that the probable causal organisms of cancrum oris are similar to those found in tropical ulcer, which is very common in the district. *C. F. Shelton*

HAN, T. N. Recidiverende zweren aan vulva en vagina gepaard met stomatitis aphthosa en conjunctivitis catarrhalis (syndroom van Behcet) bij een Chinese vrouw. [**Behcet's Syndrome in a Chinese Woman.**] *Med. Maandblad.* Batavia. 1949, Jan. 1, v. 2, No. 1, 13–17. [27 refs.]

The English summary appended to the paper is as follows :—

"A 44-years old Chinese woman suffered within a year of 10 attacks of aphthous ulcerations situated on the oral mucosa and associated with multiple sharp-edged ulcers of vulva and vagina, and a slight form of conjunctivitis catarrhalis with photophobia. The lesions appeared simultaneously or alternately at intervals of 4 to 6 weeks.

"Differential diagnosis between ulcus molle, REITER's triple syndrome, amoebiasis, STEVENS-JOHNSON's syndrome and BEHCET's syndrome is discussed. According to the author his case is identical with BEHCET's. Owing to the fact that the pathogenesis still remains obscure, it is of interest to note, that patient's husband is suffering from lung tuberculosis, that her blood globulin rate is too low (0.9 %), and that she shows gastro-intestinal disturbances (borborygmi and ructus) and anaemia."

GREEN, R. & MANKIKAR, D. S. **Afebrile Cases of Melioidosis.** *Brit. Med. J.* 1949, Feb. 19, 308–11. [22 refs.]

The authors describe a case of melioidosis in an Indian artisan in which the only manifestation was a suppurating cervical gland. Complete resolution

followed treatment by aspiration of the pus and a course of sulphapyridine by the mouth. Other workers have described similar cases in which there was no fever or other constitutional sign, the infection being confined to a solitary abscess or to superficial skin lesions.

The present authors studied the sensitivity of a strain of *Pf. whitmori* to various sulphonamides *in vitro* with results in favour of sulphathiazole and sulphadiazine. The organism is not sensitive to penicillin in concentrations attainable in the blood ; this antibiotic has been advised for local treatment. With the use of the ring-cup technique, streptomycin and polymyxin in concentrations up to 1,400μgm. per ml. failed to inhibit the growth of *Pf. whitmori*. Chloromycetin, however, in concentrations attainable in the blood (60μ gm. per ml.) gave a high degree of inhibition.

The conclusion is that chloromycetin, alone or in combination with sulphonamides, is worthy of clinical trial in melioidosis. *J. C. Cruickshank*

KAO, Yung-en. **Incidence of various Diseases among Children in Kweichow.** *Chinese Med. J.* Shanghai. 1948, Sept., v. 66, No. 9, 487–93.

ENTOMOLOGY AND INSECTICIDES : GENERAL

TAKEI, H. **Distribution and Epidemiological Significance of *Aëdes aegypti* in Kainanto.** *Kitasato Arch. Exper. Med.* 1942, Aug., v. 19, No. 2, 110–13.

DURAND-DELACRE, R. Quelques observations biologiques sur les phlébotomes de Beni Ounif-de-Figuig (Sahara oranais). [**Some Biological Observations on *Phlebotomus* in Beni Ounif-de-Figuig (Oran Sahara).**] *Arch. Inst. Pasteur d'Algérie.* 1948, Dec., v. 26, No. 4, 406–30, 6 figs. [10 refs.]

HOFFMANN, Anita. Breve nota acerca de los ectoparasitos de ratas colectadas en los mercados del Distrito Federal. [**A Short Note on Ectoparasites of Rats collected in Market Places in Mexico City.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, June, v. 9, No. 2, 81–5.

The English summary appended to the paper is as follows :—

" The author presents a brief note concerning the ectoparasites of 100 rats, collected in some of the market places of Mexico City, in June 1948. The specimens correspond to the following common species of mites : *Liponyssus bacoti*, *Echinolaelaps echidninus* ; of lice : *Polyplax spinulosa*, and of fleas : *Xenopsylla cheopis*, *Ctenocephalides felis*, *Ctenocephalides canis*, *Leptopsylla segnis* and *Echidnophaga gallinacea*."

PARROT, L. & DURAND-DELACRE, R. Notes sur les phlébotomes. LX. Quelques remarques sur les phlébotomes des terriers de Rongeurs du Sud oranais. [**Notes on *Phlebotomus*. LX. *Phlebotomus* in the Burrows of Rodents in the Area South of Oran.**] *Arch. Inst. Pasteur d'Algérie.* 1948, Dec., v. 26, No. 4, 402–5. [10 refs.]

FULLER, H. S. **Some Remarks on the Trombiculinae Ewing, 1929, in Das Tierreich, Trombidiidae, by Sig Thor and Willmann. A Critical Review.** Reprinted from *Bull. Brooklyn Entom. Soc.* 1948, Oct., v. 43, No. 4, 101–11.

MINISTRY OF HEALTH. **Memorandum on Measures for the Control of Mosquito Nuisances in Great Britain.** Memo. 238/Med. Revised Nov., 1948. 35 pp., 2 maps & 2 pls. 1949. London: H.M. Stationery Office. [9*d*.]

This memorandum was first published in 1940 and revised and reprinted in 1942 [this *Bulletin*, 1943, v. 40, 413]. The present revision retains practically all the subject matter of the earlier editions. A few deletions have been made in the section on Control; this has been modified and brought up to date by the inclusion of information on the use of DDT and BHC ("Gammexane") against mosquito adults and larvae and on the use of dimethyl phthalate as a repellent.

The memorandum mentions that only a few cases [number not stated] of indigenous malaria occurred in the British Isles immediately after the second world war [but see this *Bulletin*, 1948, v. 45, 21]. *D. S. Bertram*

DAHL, A. H. **New Plans for Vector Control in California.** *J. National Malaria Soc.* 1948, Sept., v. 7, No. 3, 231–5.

The diseases carried by arthropods which occur in California are encephalitis, fly-borne diseases, malaria, plague, Q fever, relapsing fever, Rocky Mountain spotted fever, tularaemia, and typhus fever. A new department known as the Bureau of Vector Control has been established to organize the prevention of these diseases. Its first action was to review the importance of each, the state of fundamental knowledge of the vector and the reservoir and the sufficiency of past surveys, control programmes and control demonstrations. The result of this review is set out in a table from which it is clear that work could be better balanced, and proposals are made for the increase of some items of work such as survey of encephalitis, fly-borne diseases, Q fever, relapsing fever, Rocky Mountain spotted fever and typhus, and for the decrease of others such as survey of plague and tularaemia.

The future policy of the Bureau will be guided by this analysis of the problem, and by an advisory committee. It will have a staff of 40 persons, including sanitary engineers, entomologists, sanitarians, and rodent control staff, in addition to the entomologists from the Federal agency already in the State. *G. Macdonald*

ANDREWS, J. M. **Control of Diseases propagated by Arthropod Vectors.** *Bol. Oficina Sanitaria Panamericana.* 1948, Nov., v. 27, No. 11, 998–1002. [10 refs.]

In an opening address to the Pan American Sanitary Conference of 1948 the author briefly reviews the prospects of securing efficient control of the forty diseases carried by arthropods. He concludes that barring world conflicts, especially those in which the end would seem to justify such ruthless means as biological warfare, there is every reason to believe that the present trend of arthropod-borne diseases should continue downwards. Some of these diseases seem to be susceptible to eradicative technology, certainly within the more advanced countries of the world. *G. Macdonald*

GAHAN, J. B., GILBERT, I. H., PEFFLY, R. L. & WILSON, H. G. **Comparative Toxicity of Four Chlorinated Organic Compounds to Mosquitoes, House Flies, and Cockroaches.** *J. Econom. Entom.* 1948, Oct., v. 41, No. 5, 795–801.

The authors describe tests comparing the effectiveness of DDT, benzene hexachloride, chlordane and chlorinated camphene, both as space sprays (*i.e.*

sprays intended to treat the space of a room) and as residual deposits, against house flies, mosquitoes and cockroaches.

(1) *Space spray tests.*

House flies, *Musca domestica* and mosquitoes *Aëdes aegypti* were first exposed to the spray in a 100 cu. ft. cabinet and then transferred to clean cages for recovery. The toxicity of the insecticides was compared by determining the concentration required to give 50 per cent. or 90 per cent. mortality from dosage mortality regressions. Gamma benzene hexachloride (95 per cent.) was found to be approximately six times as toxic as DDT to *Musca domestica* and two and a half times as toxic as DDT to *Aëdes aegypti*. Chlordane was slightly more toxic to house flies than DDT, but DDT was approximately three times more toxic than chlordane to *Aëdes aegypti*. Chlorinated camphene killed considerably fewer house flies and mosquitoes than the other three insecticides.

(2) *Tests with residual deposits.*

The insecticides in kerosene were applied to the inner surfaces of plywood boxes at 50, 100, 200 or 400 mgm./sq. ft. by means of a De Vilbiss atomizer. Separate samples of *Musca domestica* and *Aëdes aegypti* were exposed to these surfaces at intervals of four weeks. After thirty-six weeks, the four concentrations of DDT caused a 90 per cent. mortality to house flies and mosquitoes : Chlordane gave a 90 per cent. mortality with house flies only at a concentration of 400 mgm./sq. ft. : chlorinated camphene was effective at 200 and 400 mgm./sq. ft. against mosquitoes, but less effective against the house fly : Gamma BHC gave a relatively low mortality at all concentrations.

Further tests with mosquitoes involved spraying small outbuildings, to give a deposit of 200 mgm./sq. ft. on the walls and ceilings which were resting places of *Anopheles quadrimaculatus* and *A. crucians*. Mosquito counts were made before, and at weekly intervals after treatment, for fifteen weeks. Very few mosquitoes were found in buildings treated with DDT, but buildings treated with chlordane or gamma BHC showed increasing numbers after four weeks.

Observations on cockroaches during a month after exposure to cotton twill cloth impregnated with 200 mgm./sq. ft. of insecticide, showed that gamma BHC gave a rapid knockdown, and that gamma BHC and chlordane were effective during the first week, whereas DDT and chlorinated camphene were relatively ineffective. An infestation of cockroaches in negro dwelling houses was kept at a low level for three months by a mixture of chlordane and DDT dispersed by a thermal fog generator. *C. M. Harrison*

ALBERTO ALVARADO, C. Control de las enfermedades transmitidas por mosquitos. [**The Control of Diseases transmitted by Mosquitoes.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Dec., v. 27, No. 12, 1105–12. English summary.

MACCHIAVELLO, A. Control de las enfermedades transmitidas por pulgas. [**Control of Flea-borne Diseases.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Dec., v. 27, No. 12, 1126–37. [89 refs.] English summary.

MALO JUVERA, F. & ORTIZ MARIOTTE, C. Control de enfermedades transmitidas por piojos. [**Control of Louse-borne Diseases.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Dec., v. 27, No. 12, 1113–25. [11 refs.] English summary.

DIAS, E. Contrôle das doenças transmitidas pelos triatomas. [**Control of Diseases transmitted by Triatomas.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Dec., v. 27, No. 12, 1160–64. English summary.

KALMBACH, E. R. **Observations on New Rodenticides.** *Bol. Oficina Sanitaria Panamericana.* 1948, Dec., v. 27, No. 12, 1138–47. [11 refs.]

ESTRELLA R., J. A. Observaciones sobre nuevos rodenticidas en Perú. [**Study on New Rodenticides in Peru.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Dec., v. 27, No. 12, 1148–9. English summary.

LABORATORY PROCEDURES

SUTER, R. Action des " produits mouillants " sur la coloration des parasites sanguicoles. (Note préliminaire.) [**The Use of Wetting Agents in the Staining of Blood Parasites.**] *Ann. Parasit. Humaine et Comparée.* 1948, v. 23, Nos. 3/4, 220–21.

Swiss work had previously shown that " thedan blue " was an ideal and rapid stain for certain blood parasites (trypanosomes, spirochaetes and leptospira) [see SIMONS, this *Bulletin*, 1947, v. 44, 628]. The stain is composed of methylene blue and saponin which form a stable combination. The saponin haemolyses the red cells and thus makes it easy to detect the organisms even when very few are present. Under ordinary illumination, the parasites stain blue but under the dark ground, the curious " Berek effect " is produced and the organisms exhibit an intense and brilliant red colour.

The author discovered that saponin could be replaced by many other wetting agents as long as they possessed a haemolytic action. Two were found which acted nearly as well as saponin —Desogene (a quaternary ammonium compound) and Eriopon (an amide prepared by Geigy). *P. C. C. Garnham*

GOLDMAN, M. **A Single Solution Iron-Hematoxylin Stain for Intestinal Protozoa.** *Stain Technology.* 1949, Jan., v. 24, No. 1, 57–60.

Two solutions are prepared :—

Solution A.—A 1 per cent. solution of haematoxylin in 95 per cent. alcohol prepared by diluting a 10 per cent. stock solution of the dye in 95 per cent. alcohol. Ripening is unnecessary.

Solution B.—Ferric ammonium sulphate 4 gm., glacial acetic acid 1 cc., concentrated sulphuric acid (sp. gr. 1·8) 0·12 cc., in 100 cc. of distilled water.

Equal parts of freshly prepared solutions of *A* and *B* are mixed and kept for a few hours and filtered before use. The mixture should be discarded if it becomes greenish black in colour, instead of dark brown.

Faecal films are fixed in Schaudinn's solution plus 5 per cent. acetic acid, for 1 hour, washed in 70 per cent. spirit plus iodine for 5 minutes and then in 2 changes of 50 per cent. spirit for 3 minutes each. The stain is applied for 3 minutes and washed off in tap water for 5–30 minutes. The film is finally dehydrated, cleared and mounted.

Intestinal protozoa are stained blue or grey and show the usual features brought out by the Heidenhain technique, though with less precision. The method is recommended for routine diagnostic purposes. *P. C. C. Garnham*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

COLONIAL OFFICE. **Report of the British Guiana and British Honduras Settlement Commission.** Cmd. 7533. [EVANS, Geoffrey, Chairman.] pp. viii + 359, 10 maps (9 in pocket and 1 in text) & 3 text figs. 1948. London : H.M. Stationery Office. [7*s.* 6*d.*]

The public health as well as the social and economic structure of the West Indian islands reflect the difficulties caused by excess of population, the density of which varies from 1,200 to the square mile in Barbados to a little below 300 in Jamaica and Trinidad. In contrast, the enormous territories of British Guiana and British Honduras are virtually unpopulated, with densities of 4½ and 7 per square mile respectively. In each of these last two there is a small, densely populated area with a vacant hinterland isolated by a natural barrier of difficult country which has prevented free access.

There have been many suggestions for the use of these vacant lands, and this Commission was instructed to report on the possibilities of settlement in them " having regard to the recommendations made by the West Indian Conference in 1944 and 1946 regarding the need for study of the Guianas and British Honduras as an aid to the solution of the problem of over-population in the West Indian island territories. . . ." The report makes it clear that there is no insuperable barrier to settlement. Medical problems are examined in detail. An analysis of the history of British Guiana shows that until recently the death rate exceeded the birth rate and the population was only maintained by regular immigration, though some doubt is thrown on the normally-accepted estimate of the extent of the natural decrease. In recent years a natural increase has replaced the decrease and it is reliably estimated that the population will increase by 40 per cent. in the next 15 years. Malaria, once the greatest cause of mortality, is no longer so, and there is no other serious endemic disease which cannot be brought under reasonable control either in the coastal lands or in the interior. An able analysis of the effect of the climate on Europeans shows that there is no reason why they should not live and work there in what is called sporadic or dependent settlement, as technical advisers and administrators ; but close or independent settlement by them is not advisable.

The Commission considered the two alternatives of encouraging the independent settlement of smallholders and of large-scale commercial plantations without considering any intermediate type such as co-operative farming on an economic scale. The decision is in favour of encouraging agrarian settlement for the production of export crops on a plantation, not a smallholding, basis, immigration being timed to meet the needs of the various projects. Most immigrants would arrive as contract employees of individual concerns, the large employer so far as possible providing housing and social services, though Government would care for smallholders in this way.

The many difficulties are reviewed and it is concluded that it should be possible over a period of some ten years for the two Colonies to absorb about 100,000 men, women and children, including about 25,000 adult workers. Such migration would have to begin slowly and extend over many years and would lead, it is hoped, to a " chain reaction " of economic progress in the economy of the two Colonies which would continue to absorb immigrants.

[The reviewer cannot avoid the feeling that the Commission has overlooked the instruction to consider the matter as an aid to the solution of the island population problem. Though the health, economics and population of these two Colonies are closely studied there is no factual matter besides a brief introductory note on the relation between the rate of increase in the population in the islands and the absorptive capacity of the new countries. Details are given of the proposed Development Corporations and of the intentions for agricultural development, but the estimate of the number who could be absorbed is baldly stated in the introduction without any supporting data in the text on the rate of migration or the manner in which the total has been estimated. It may be that the Commission considers that immigration would only start on any material scale in the last couple of years of the decennium, and a rapid increase might be expected thereafter. Perhaps the figures given refer to direct employees and their dependents only and the total would be swollen by an equal number engaged in trade, transport, ancillary services and the professions. Perhaps a plantation area is considered only as a nucleus for the growth of those services needed by a farming community which would appear around them. But on these points and similar relevant ones the Commission throws no light. The question whether settlement in the interior is possible is adequately answered in the affirmative. The question whether such settlement could have any material effect on the population problems of the islands is left unanswered.]

G. Macdonald

FORD, J. & HALL, R. de Z. **The History of Karagwe (Bukoba District).** *Tanganyika Notes & Records.* 1947, Dec., No. 24, 27 pp., 1 map. [29 refs.]

The authors are interested in the history and especially in the early epidemics of a part of Bukoba, a district in Tanganyika lying along the south-west corner of Lake Victoria.

Bukoba is inhabited by two very different tribes. The Bahima, who are aristocratic pastoral people, Nilotic in origin and the Banyambo, who are agricultural people and Bantu. In the latter part of last century there was a long period of serious raiding, wars and disturbances, aggravated by European penetration, though the authors state that German occupation was not seriously harmful to the social organization of the country. At the same time there was a serious uncontrolled epidemic of smallpox which was apparently a disease new to the country, and chiggers (*Tunga penetrans*) arrived from West Africa. As the people did not understand how to deal with the chiggers many men were crippled and in some places harvests were lost because the people were suffering from chigger ulcers and could not get the crops in.

The country had been prosperous for grass was good and there were plenty of good cattle. In 1890 or 1891 there was an immense epizootic of rinderpest with terrible destruction of the cattle. The Bahima were compelled to fall back on the crops produced by their agricultural neighbours and dependents. They lost their social position by doing so but were saved from death by starvation. It seems that until the end of last century tsetse flies were absent: then *G. morsitans* entered the country apparently from the south, and by 1909 had advanced at least seventy miles, crossing the border into Ankole where cattle died and trypanosomes were found.

The result of all these disasters was serious loss of population, and the people who remained were socially disorganized. As the cattle died the grass country went back to bush and became occupied by tsetse. At present the reduced population is concentrated and the people are somewhat crowded together as a measure against the risk of sleeping sickness. The authors point out that there have been many causes operating to ruin this good land. Among them is the fact that the indigenous society was not well adjusted to meeting strains [a somewhat indefinite diagnosis].

The authors have assembled a large amount of information which is of necessity fragmentary; they seem to have interpreted it in a reasonable way. The result is a refreshing and interesting paper. *P. A. Buxton*

MINISTRY OF SUPPLY & DEPT. SCIENT. & INDUST. RES. **Tropic Proofing. Protection against Deterioration due to Tropical Climates.** Compiled by the Directorate of Chemical Research and Development. pp. iii + 32. 1949. London: H.M. Stationery Office. [9*d*.]

The work was originated by the Ministry of Supply in the war period. Studies were made on the destruction of military equipment of many types by insects and fungi and tropical climates: also on methods of protecting equipment or designing it in such a way as to reduce damage. Work on these subjects is still in progress in Nigeria.

The present pamphlet is brief and rather general. It deals with attack by fungi and insects and discusses the particular problems of a great variety of materials, among them plastics, leather, wood, textiles, paper and paints. The special problems provided by optical and electrical instruments are also considered. Damage done to buildings, ships or other large structures or to foodstuffs is not included.

The account of fungi covers four pages. The main biological characteristics of the moulds are introduced and attention is directed to conditions of temperature and humidity which are generally most favourable to them. It is pointed out that some moulds may interfere with the performance of optical instruments owing to the presence of their hyphae on the surfaces of lenses or mirrors: others may grow through the insulation of electrical devices or bridge gaps in circuits. Other moulds grow, as is doubtless well known, on organic materials of many types, and some of the species are particularly associated with certain substrates. The section on fungi is concluded by brief and rather general recommendations about the reduction of damage.

It is considered that damage by insects is a relatively minor matter and the whole subject is dealt with in about a page and a half. This seems inadequate: for instance it is not possible to deal with the biology of termites and the damage they cause in one paragraph. One observes also that in describing the destruction of woollen materials by beetles there is no reference to the organic insecticides.

A number of other criticisms might perhaps be made. One would expect some reference to the possible toxic action of certain of the fungicides to the men who apply them. We feel also some doubt about a list of timbers which are said to be resistant both to fungi and to termites: it would surely be preferable to distinguish two groups of timbers and if possible to identify them by their scientific names. In the present list each timber is given only a single African or Asiatic name. Parts of the pamphlet appear to have been drafted by someone who experienced great difficulty in expressing his meaning in English, though the sympathetic reader will generally divine what is intended, as in the following example:—

> " . . . stores containing rubber parts should, therefore, be given a fair chance and should not be exposed unnecessarily to heat, brilliant sunlight or to other adverse conditions. An interesting, and unexpected, example of this is the formation of high concentrations of sulphuric acid in imperfectly drained hose, due apparently to certain strains of thiophilic bacteria."

The subject of the pamphlet is without doubt very important. A greatly extended edition of it with a fuller list of references might well be a very valuable work. *P. A. Buxton*

IRIARTE, D. R. Estudios entomologicos y parasitologicos. [**Entomological and Parasitological Studies.**] 253 pp., numerous figs. & 3 coloured folding pls. 1948. Caracas: Tipografia Americana.

This is a collection of articles, most, if not all, of which have been published before and all but two have already received notice in this *Bulletin*. The longest is the first, on the Simuliidae of Venezuela. In this the author reviews the history of the Family and gives an account of their bionomics; one section is given up to the question of their classification and contains a description of the 11 species already found by the author in Venezuela and a useful key for their identification. Six other species have not been found by the author himself; of these he, therefore, gives the original descriptions. Line maps indicate the distribution of these species. Finally, there is a fairly comprehensive bibliography on the subject. Other papers, dealing with cutaneous leishmaniasis, Chagas's disease, carate and paracoccidiosis have already been abstracted in this *Bulletin* [1940, v. 37, 105; 1945, v. 42, 655; 1946, v. 43, 1128, *et al.*] and need not be again referred to. *H. Harold Scott*

BOOK REVIEWS

SIPPE, George [M.B., B.S. (Syd.), Acting Senior Pathologist, Colonial Medical Service]. **Nutritional Macrocytic Anaemia.** 76 pp., 13 pls. (3 coloured & 2 maps) & 16 charts, 1947. London: Crown Agents for the Colonies, 4 Millbank, S.W.1. [£1 1*s*. 0*d*.: *Rs*. 14.]

This volume bears the date 1947 and was received for review in December, 1948, but it is only fair to the prospective reader, and to the author, to say that it contains intrinsic evidence of having been a very long time in the press: for example, there is only one reference dated 1943 and none with a later date, and the words "folic acid" were not encountered.

With the limitations naturally associated with the above facts, the book constitutes a useful, but of course far from complete, summary on nutritional macrocytic anaemia and gives some indication of the type of case that is encountered in Mauritius. However, if this information had been condensed into a paper of 3,000 to 5,000 words and published in a medical journal at the end of 1943 or early in 1944, it would have constituted an up-to-date and far more useful contribution to the literature on this subject.

The condition is common in Mauritius and most common in the highly malarious coastal belt, but no general survey has been done. The author found macrocytes in 20·3 per cent. of 300 blood slides taken from children.

The stable diet of members of the labouring classes, from among whom all the cases came, is parboiled rice, 485 grammes daily with pulses (40 grammes), bread (62 grammes), and fruit and vegetables when they are in season and cheap. They consume about 16 grammes of fat, mostly vegetable in origin. Meat is eaten rarely, less than once a week, and fish "occasionally" but "milk is drunk regularly": it is stated that this is usually diluted but there is no indication of the average amount taken. The common vitamin deficiencies are A and B groups.

Splenomegaly was found in 75·9 per cent. of the cases and the usual cause was malaria. The van den Burgh reaction was 1·0 mgm. or over in 22·2 per cent and 0·5 mgm. in 51·1 per cent. of cases; of the former group 90 per cent. of patients had enlarged spleens.

"Malaria appears to exert its destructive influence partly by direct parasitization of the red cells, partly by a toxic effect on the bone marrow, but mainly by hypertrophy of the reticulo-endothelial system, which then attacks the abnormal erythrocytes." This statement is not based on his reported experience.

"Whilst the disease in its severe form does appear to be definitely more common in females, particularly during pregnancy, there is no evidence that there is any particular age or sex distribution of mild or moderately severe nutritional macrocytic anaemia. Thus, in Mauritius, macrocytosis and mild clinical anaemia was found commonly in children under 10 years and the male: female ratio was approximately 1 : 1.

"Eighty per cent of the local cases were Hindus," but the percentage of Hindus in the population group is not here stated: elsewhere it is noted that "the labourers . . . are mostly Hindus."

The months of highest incidence of severe anaemia are June, July and August, whereas the malaria season is from February to May. The author thinks that the former disease is dependent on the latter.

The pathology of the disease is discussed from the literature: no new data are supplied.

The clinical picture is described: it is not always clear whether the author is giving his own experience or quoting from the literature. In his cases,

abdominal pain is common (50 per cent.) and vomiting less frequent (25 per cent.). Wasting is unusual. Tachycardia is usual but not hypotension. Nervous symptoms are few and there was never any cord involvement.

Some mean blood findings in the cases were as follows :—

Haemoglobin, grammes per cent.—4·08 (1·41 to 12·85)
Red cells, per cmm.—1,129,000 (lowest 375,000)
Mean corpuscular haemoglobin—37·35
Mean corpuscular—haemoglobin concentration—28·8 per cent.
Mean corpuscular volume 134·7 cu.μ.
Mean corpuscular thickness—4 of 10 above 2·5 μ.
Mean corpuscular fragility (non-pregnant cases)—0·349 Na cl.
Leucocytes per cmm.—4,530
Platelets per cmm.—77,038 (17,850–154,840).

In the sternal puncture smear the author found normoblasts and megaloblasts: the latter were of about the same average size as those found in pernicious anaemia [and larger than other workers have reported in nutritional macrocytic anaemia]. The ratio of red/white precursors was about 1/1.

The Price-Jones curve shows a shift to the right in most cases.

The three curves illustrated show a higher peak and narrower base than is typical of pernicious anaemia.

The mortality rate was approximately 18 per cent.; late application for treatment was the main cause of this high mortality. The author devotes a chapter (or rather a part) to treatment, but again it is difficult to follow what he himself actually used in his cases, except that in six (4 males and 2 non-pregnant females) he used a locally prepared yeast mixture, a by-product of a local sugar factory. These six cases are reported in detail and, in 4, graphs of the blood counts are given; all showed rapid and satisfactory improvement. [However, the treatment of pregnant women constitutes a much more difficult problem.] The author refers to whole liver, liver extracts, and Marmite, but not to proteolysed liver or folic acid. He also mentions blood transfusion, but not apparently from personal experience in this disease.

There are three short appendices: on Mauritius, with a map; on technique, in which he notes the methods he used: and a table of the blood findings in his fifty cases.

The book is generally speaking well produced and contains a number of illustrations, including two good coloured plates of megaloblasts, but it is not entirely free from printing (or clerical) errors: *e.g.*, there is a reference to WILLS and MAWSON which should obviously be MILLS and MAWSON, and Machanda, Manchanda, and Manchunda, are variants used to indicate one worker.

L. E. Napier

MATHIS, C. [Membre correspondant de l'Académie de Médecine, etc.] & PONS, R. [Ancien Chef de Laboratoire à l'Institut Pasteur de Saïgon, etc.]. **Manuel de Pathologie Exotique.** [Manual of Tropical Diseases.] pp. viii+642, 10 figs. & 1 coloured pl. 1948. Paris: Presses Universitaires de France, 108 Boulevard Saint-Germain. [35*s.* 6*d.*]

This book is intended primarily for the use and guidance of medical practitioners in the Tropics. It covers the whole range of diseases commonly dealt with in text-books of tropical medicine. In every chapter attention is mainly concentrated on clinical signs and symptoms, diagnosis and treatment. Descriptions of laboratory techniques essential to the diagnosis of so many tropical diseases are confined to those which the average practitioner should be capable of carrying out himself. Preventive measures receive but scant attention. Notes concerning the geographic distribution of diseases relate almost entirely to French overseas possessions.

The book is clearly and concisely written and very well produced. It is evidently based on wide personal experience, but the authors' claim that their manual takes count of recent advances in knowledge of the aetiology and treatment of tropical diseases can hardly be substantiated. Omissions are very numerous: for example, new methods of malaria therapy receive bare mention and the yellow fever chapter is very inadequate.

Rapidity of progress in the domain of tropical medicine has been so great during the last ten years that the difficulties attendant upon the production of an up-to-date manual are almost insurmountable. The major part of this volume would appear to have been written several years ago. Very considerable additions would be necessary for the adequate discharge of the authors' self-imposed task.

Norman White

KUCZYNSKI, R. R. **Demographic Survey of the British Colonial Empire. Vol. 1. West Africa.** pp. xiii+821. Issued under the auspices of the Royal Institute of International Affairs. 1948. London: New York: Toronto: Geoffrey Cumberlege, Oxford University Press. [75*s*.]

The first volume of this Survey deals with West Africa. It is packed with a wealth of statistical and other documentary detail, attractively presented and constructed throughout against a historical perspective.

The book is introduced with seven sections dealing with the fundamentals, namely Census-taking; Total Population; Composition of Native Population; Composition of Non-Native Population; Birth and Death Registration; Native Fertility, Mortality and Population Growth; and Mortality of Europeans.

This sequence is followed in each of the main chapters which deal respectively with Sierra Leone, Gambia, Gold Coast and Togoland, and Nigeria and the Cameroons.

Of special interest to medical readers will be the large amount of material dealt with under the various headings of "mortality", which concerns the common infective and other diseases of the Tropics. The great part of this material is taken from Annual Medical Reports of the Colonies and from similar sources but its assembly against this background gives it a renewed appeal. The Survey contains an immense amount of information which will be of value and interest to those who are concerned with West Africa and its welfare.

H. J. O'D. Burke-Gaffney

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